Social Judgment and Risky Decision Making in Huntington's Disease

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DECLARATION

" This thesis has been composed by myself and the work contained herein is my own."

ABSTRACT

Huntington's Disease is an inherited neurodegenerative disorder, associated with problems in judgment and decision-making. The extent of these problems, and their association with clinical characteristics has however, only recently been assessed (Stout, Rodawalt, Siemers, 2001). Parallels are often drawn between the behavioural disturbances in Huntington's disease and those observed with damage to the frontal lobes. Indeed an anatomical basis for these similarities does exist because of the connectivity of the basal ganglia and the frontal cortex, within several frontal-subcortical circuits (Cummings, 1993).

In view of these identified similarities, this study aimed to examine decision-making deficits in individuals with Huntington's disease and asymptomatic disease gene carriers using a laboratory-based simulated gambling task. This task has been used to quantify similar decision-making deficits in ventromedial frontal lobe damaged participants (Bechara, Damasio & Anderson, 1994). Judgement deficits were assessed using a theory of mind test, examining the ability to recognise a faux-pas. This test has been used to assess deficits in individuals with damage to the orbito-frontal cortex (Stone, Baron-Cohen, & Knight, 1998).

For this study, 14 symptomatic, 10 asymptomatic, and 13 controls completed the simulated gambling task, the faux-pas task, and a neuropsychological test battery. It was hypothesised that both symptomatic and asymptomatic Huntington's disease participants would demonstrate deficits in comparison to controls on the gambling task and the faux-pas task. Results are discussed with reference to previous research findings.

CHAPTER ONE

INTRODUCTION

1. 1 GENERAL INTRODUCTION

Huntington's disease was first described by George Huntington in 1872 (Huntington,1972) based on data gathered by himself, his father, and his grandfather on families living in Huntington County New York. Although descriptions of persons with chorea appeared in the medieval literature, and Sydenam, some 300 years ago described acute chorea as part of the syndrome now known as Rheumatic fever (Nausieda, 1986), Huntington was the first to describe the features of the genetic disorder that now bears his name.

The international prevalence of Huntington's disease is 1:10,000, and it is inherited as an autosomal dominant disorder. Therefore statistically 50% of the children of heterozygotes for the Huntington's disease gene will themselves inherit the gene and therefore the disease.

The mean age of onset of the Huntington's disease symptoms, is between 35 and 44 (Hayden, 1981; Bruyn & Wendt, 1986; Folstein, 1989; Harper, 1996) thus many people make childbearing decisions prior to symptom onset. However Huntington's disease onset can range from 2 years to later than 80 years, although onset before the age of 10 and after age 70 is rare.

Approximately 80% of individuals with juvenile onset inherit the disease from their father, and elderly patients are more likely to have inherited the gene from their mother (Bruyn & Wendt, 1986; Harper & Shaw, 1996). Inheritance through the father can lead to earlier onset through succeeding generations, a phenomenon

termed anticipation. However if the disease is not inherited by the child of a carrier, this is where the disease line stops.

HD is a neurodegenerative disorder which causes preferential loss of neurons in the basal ganglia, in particular the caudate nucleus and the putamen (VonSattel et al., 1985). It is characterised by the progressive loss of control over three primary functions: motor control, cognitive control and emotional control.

As there is a genetic basis for the disease, it is therefore a disorder of families, because a person either develops HD or experiences the presence of HD in multiple relatives. Much of the research with people with HD or gene carriers who have yet to develop the disease has focussed on motor and cognitive functions. Personality and psychiatric functioning in HD have been researched less extensively. This is despite the fact that a frequent complaint expressed in a clinical setting is that people with HD, regardless of their premorbid personalities, display poor judgement as well as changes in their social behaviour.

More recently Stout and colleagues assessed these highlighted problems in judgement and decision making, and their association with clinical characteristics (Stout, Rodalwalt, & Siemers, 2001). The current study was undertaken and employed a similar technique to assess decision making deficits in people with HD. Also assessed were deficits in social judgement. Asymptomatic gene carriers (people who have yet to display the clinical symptoms of the disease) also completed the assessments. Neuropsychological research has highlighted that cognitive deficits may be detected preclinically in asymptomatic gene carriers, so the current research examined if there are quantifiable judgement deficits also present prior to the onset of clinical symptoms of the disease.

1. 2 HUNTINGTON'S DISEASE

1. 2. 1 GENETIC TESTING

Huntington's disease was the first serious autosomal dominant disorder for which genetic prediction became possible using DNA markers. The genetic marker for Huntington's disease was localised in 1983 to a DNA marker on chromosome 4 (Gusella et al., 1983). The discovery of this marker for Huntington's disease made possible the use of linkage analysis to identify currently unaffected carriers with a sensitivity of about 96-99%.

Linkage analysis takes advantage of the spatial proximity of a marker and a mutation and requires blood samples from both affected and unaffected family members over several generations. There were problems with the linkage analysis because genetic recombination can occur between markers and the gene during meiosis. Most carriers were given risk assessments of 90% or more and most non-carriers were given risk assessments of 10% or less, reflecting the relatively low accuracy of these earlier linkage studies.

The identification of a specific mutation for HD (Huntington's Disease Collaborative Research Group, 1993) and the recognition that essentially all cases resulted from the same mutational mechanism of trinucleotide repeat expansion, provided a presymptomatic test that was highly accurate (Macmillan et al., 1993; Kremer et al., 1994). This test has a sensitivity and specificity of virtually 100%.

Impact of Genetic Testing

When linkage analysis first became available there were concerns that predictive testing could lead to an increase in death by suicide among identified carriers. Suicide has long been recognised as a serious consequence of Huntington's disease. One study reported a four-fold increase in the suicide rate among people affected compared with the rate of the general white population in the United States (Farrer, 1986). Attitudinal surveys suggest that between 11% and 33% considered suicide a possible response in the future (Mastromauro, Myers, & Berkman, 1987). This data highlighted the need for research to identify predictors of depression and suicidal intention in people entering predictive testing programmes for Huntington's disease.

Meiser & Dunn (2000) reviewed the literature on attitudes to, and the psychological impact of testing for the disease. Most of the evidence suggests that non-carriers differ significantly in terms of short term but not long term, general psychological distress. Indeed their review suggested that psychological adjustment prior to testing rather than the test result itself was more predictive of psychological adjustment after the test.

However it is important to note that only 10-20 % of people at risk for Huntington's disease actually take the test (Babul et al., 1993). Thus because of this relatively low rate of uptake, it is likely that people who chose to be tested are not representative of the Huntington's disease population as a whole (Tyler, Ball & Crauford, 1992).

Several studies have provided evidence that people who choose to be tested are psychologically selected for a favourable response to testing. The most commonly

reported reasons for choosing not to have the test related to the emotional and psychological consequences of a positive test result-such as fear of searching for symptoms and of losing what hope could be retained (Babul et al.,1993).

Therefore the evidence on self-selection for a favourable response of people who choose to have the test, suggests that findings of studies on the psychological impact of genetic testing, may not be generalised to the population of people at risk of Huntington's disease at large. It is worth noting that all of these investigations were carried out in settings where intensive counselling protocols were in place and eligibility was tightly controlled. The impact in settings where there aren't these protocols intact is unknown, and thus the authors concluded that testing is best offered as part of comprehensive specialist counselling. Given the potential psychological sequalae of genetic testing in less well-adjusted people, it is advisable to routinely assess levels of depression or hopelessness with formal assessment tools (Beck et al., 1990). People with high rates of depression may benefit from referral to specialist services i.e. Clinical Psychology or Psychiatry.

Tibben and collegues also followed up the partners of people undergoing genetic testing, and found that carriers' partners showed the same course of distress as carriers; showing significantly higher levels of distress than the partners of non-carriers at 1 week, 6 months and 3 years (Tibben, Timman, Bannink, & Duirenvoorden, 1997). Having children was an additional psychological risk factor for carriers' partners. These findings suggest that partners need to be included more comprehensively in psychological assessments (Hayes, 1992).

1. 2. 2 THE DIAGNOSIS, AND DISORDERS OF HUNTINGTON'S DISEASE

The clinical diagnosis of the disease is based on family history and the onset of choreiform movements (Harper, 1992). The development of these adventitious movements is gradual (Hayden, 1981; Bruyn & Wendt, 1986; Folstein, 1989; Harper, 1996) and they are usually accompanied by personality change. Indeed Huntington's disease is characterised by the progressive loss of three primary functions: motor control; emotional control; and cognitive function, which are described below.

(i) THE MOTOR DISORDER

The disorder of movement in Huntington's disease has two components: involuntary movements and abnormalities of voluntary movement. The involuntary movements are most commonly choreic, but motor restlessness, myoclonus, dystonia, and athetosis may also be seen. Voluntary movement is impaired by clumsiness, bradykinesia, slowing of response time, and the inability to sustain a voluntary movement, and is thus similar in some ways to Parkinsonism. Involuntary movements usually predominate early in the illness, but these may gradually diminish late in course, giving way to a rigid akinetic state. There is evidence from physiologic and pharmacologic studies that voluntary and involuntary movements actually constitute two separate movement disorders. These disorders of movement are briefly defined in the involuntary and voluntary categories.

Involuntary Movements

A variety of involuntary movements occur in HD. It is not clear whether these involuntary movements have the same or different pathophysiologic mechanisms. Marsden (1984) reported that HD patients with chorea can have electromyograms

typical for chorea, myoclonus, or dystonia. Clinically the chorea, myoclonus, and dystonia are quite different, and it is important to recognise that all may be seen in HD, sometimes in the same patient either at the same examination or at different times during the course of illness.

Chorea- meaning dance, is characterised by sudden, quick, unintended movements of almost any body part. It is not stereotyped or repetitive. Early in the illness, choreic movements are usually low in amplitude and occur in the distal body parts especially the hands and feet. However as the disease progresses the movements become more frequent and pervasive and of higher amplitude, usually reaching a peak of severity about 10 years after onset. Following this, involuntary movements either plateau or lessen and may disappear in patients who survive for 15 years, except when the patient is stimulated (Folstein, Leigh, Parhad, & Folstein, 1986). Voluntary movement and psychological stress differentially influence the expression of chorea. Chorea is worsened by a stressful task, and lessened by voluntary movements such as writing or talking.

Motor Restlessness- this often begins prior to the onset of choreic movements. Individuals tend to be unaware of these movements, however families report that patients gesticulate more, are unable to sit quietly, and appear anxious or nervous.

Dystonia- dystonic posturing is when patients hold up an arm, or leg, or hold the upper body in an awkward position. It can coexist with chorea or motor restlessness or may be seen alone, it can occur at any time during the course of the illness, but is most severe in advanced stages of the disease, when the body becomes permanently twisted after years of severe dystonia.

Tremor and Myoclonic Jerks- Patients at risk for the disease may display a fine tremor, when they hold their arms extended. Folstein (1989) reported that it often appears to be related to caffeine, alcohol, or other drug intake, and it is not observed consistently from year to year. Myoclonic jerks are rare but can be seen in children and adolescents with HD and patients with advance disease.

In summary, chorea is by far the most common involuntary movement seen in HD, although duration varies considerably from case to case. Motor restlessness can precede frank chorea. Mild dystonia commonly accompanies chorea and motor restlessness; but dystonia can become severe (as may tremor and myoclonus) in those with advanced disease.

Abnormalities of Voluntary Movement

HD patients also have abnormalities of voluntary movement, which includes a general slowing. The voluntary motor acts are bradykinetic and clumsy, motor activity cannot be maintained over a period of time (motor impersistence) and there is often a lag before the initiation of voluntary movement (motor latency). Voluntary motor impairments in HD are demonstrated most clearly in the examination of eye movement and is also observed in coordination, gait, speech and swallowing (Folstein, 1989).

Motor Findings in End Stage HD

Toward the end of life, involuntary movements usually lessen, leaving the patient in a state of akinetic mutism. Some family members describe patients in this state as "locked into their bodies". The patients have also been cited as examples of a persistent vegetative state (Walshe & Leonard 1985).

Summary of Movement Disorder in Huntington's Disease

The most easily observable motor abnormality in HD is chorea. It may however be absent or overshadowed by other involuntary movements such as tremor and motor restlessness, bradykinesia or clumsiness of voluntary motor movements. Voluntary and involuntary movement abnormalities are likely to be related to different subsystems within the basal ganglia and must be considered separately when studying pathophysiology and documenting the response to treatment.

(ii) THE EMOTIONAL DISORDER

The initial symptoms of HD are extremely variable. They can be motor, cognitive, emotional/behavioural, or any combination of all three. Patients commonly exhibit psychiatric disorder several years before other symptoms begin. This type of presentation is reported in as many as half of the cases in some case series (Heathfield, 1967; Mattson, 1974). Common presenting emotional symptoms are depression, irritability and apathy.

Individuals with HD may present with affective disorders i.e. depression/anxiety, (Folstein, Franz, Jensen, & Folstein, M.F, 1983); personality change, (Shoulson, 1990); and psychotic symptomatology including hypomanic spells and frank mania (Folstein, 1989). Affective syndromes are most commonly seen early in the course of the illness.

Personality and psychiatric functioning in HD have received far less attention than motor and cognitive functions; however there is ample evidence of a variety of such behavioural disturbances in HD.

There have been parallels drawn between the behavioural disturbances in HD and those observed with damage to the frontal lobes (Cummings, 1993; Jacob & Huber, 1992; Mega & Cummings, 1994). Indeed there is an increase in levels of non-violent crime in men with HD compared to their non-affected 1st degree relative (Jensen, Fenger, Bowig, & Sorenson, 1998). In a clinical setting a complaint frequently expressed is that people with HD display poor judgement as well as other changes in personalities and social behaviour (Stout et al., 2001).

Indeed an anatomical basis does exist for the similarities in the behavioural disturbances which occur in HD and frontal lobe damage which will be later described.

(iii)The Cognitive Disorder

Huntington's disease patients have a dementia (i.e. a global cognitive decline in clear consciousness), but they do not have aphasia or agnosia and rarely apraxia, the cardinal features of the dementia of Alzheimer's disease. The dementia of HD is one of the dementias considered to be sub-cortical. Subcortical dementias are characterised by a memory defect, cognitive slowing, apathy and depression, but a sparing of the ability to comprehend and express language (McHugh & Folstein 1973; Albert, Feldman & Willis, 1974).

There has been extensive research carried out examining the cognitive deficits in HD. The results of this research have been inconclusive and inconsistent. Zakzanis (1998) used meta-analytic principles to review neuropsychological findings in patients with HD in studies dating back to 1980. The goal of their review was to estimate the consistency, strength, and selectivity of neurocognitive deficits in HD using meta-analysis and to rank-order the tasks and term variables in terms of

sensitivity to cognitive alterations in HD. The literature on HD was also organised into superordinate neuropsychological domains to aid in the interpretation of data. The results indicate that patients with HD are most deficient on tests of delayed recall, followed by performance on measures of memory acquisition, cognitive flexibility and abstraction, manual dexterity, attention/concentration, performance skill and finally verbal skill (Zakzanis, 1998).

The Measurement of Specific Cognitive Deficits in Huntington's Disease

Delayed Recall

The tests of delayed recall corresponded to the largest obtained effect size compared to the other neuropsychological domains. More specifically verbal and visual delayed recall on the Logical Memory and Visual Reproduction subtests of the Wechlser Memory Scale-Revised (WMS-R; Wechlser, 1987) are the two most sensitive neuropsychological tasks for indexing cognitive dysfunction in HD. Zakzansis (1998) stated as has been stated elsewhere (Folstein, 1989), that the poor performance may not have reflected a severe memory impairment because patients perform relatively well when memory is tested in a recognition format. Thus patients with HD may only have a mild to moderate memory impairment that results from a retrival deficit due to frontal-striatal dysfunction (see Brandt, 1993; Brandy & Rich, 1995).

Memory Acquisition

This was measured using the Californian Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987) which demonstrated that memory acquisition tasks were next most sensitive to HD impairment. Again however the magnitude of these particular memory acquisition tasks does not reflect severe memory impairment when the qualitative nature of the disease is taken into account (Zakzansis, 1998).

Cognitive Flexibility and Abstraction

This was measured using the Wisconsin Card Sorting Test (WCST; Heaton, 1981), and performance on this task was able to discriminate 82 % of patients with HD from healthy controls. The pattern of performance was consistent with the widespread cognitive alterations expected from frontal-subcortical circuit dysfunction (see Cummings, 1993) and not with the effects of an isolated dorsolateral prefrontal lesion (see Stuss & Benson, 1984; 1986). Impairments were also demonstrated on the Tower of London (Shallice, 1982) and phomemic word fluency measured using the Controlled Oral Word Association Test (COWAT; Benton & Hamsher, 1989). Overall the cognitive flexibility and abstraction domain was more impaired in HD compared to the remaining domains (Zakzansis, 1998).

Manual Dexterity

Given the presence of choreiform movements and in keeping with the subcortical neuropathology of HD, performance on tasks of manual dexterity were impaired as expected. Surprisingly, however the obtained effect size for right-hand performance on the Purdue Pegboard (Lezak, 1995), the Grooved Pegboard (Lezak, 1995) and the Finger Tapping Test (Reitan & Wolfson, 1993) were all considerably larger then those obtained on the same tasks for the left hand or bilateral conditions.

One could conclude from these results that there is an assymmetrical deficit, however the authors argued that the magnitude of the obtained effect might reflect the blatant behavioural asymmetry observed in 'normals' who prefer to use-and are thus more dexterous-their right hand (see Heilman, 1997). This would in turn inflate the difference in performance on tasks of manual dexterity between healthy normal control subjects and patients with HD more so for the right than the left hand. However, is needed to clarify the present pattern.

Attention and Concentration

Tests of attention such as Trail Making Test Parts A and B (Lezak, 1995) are moderately impaired in HD. More specifically performance on Part A was similarly impaired to Part B. Performance on the Stroop tests (Lezak, 1995; Stroop, 1935) is more sensitive to the attention/concentration deficit in HD. Colour reading is the most sensitive, followed by Stroop colour-word reading, followed by word reading with colour inhibition. Again the pattern of results is consistent with generalised cognitive slowing, rather than a core deficit of some failure of selective attention or failure of response inhibition (Lezak, 1995).

The research also set out to investigate if there was any relationship between neuropsychological impairment and clinical and demographic attributes of patients with HD, and none were found in the quantitative review completed by Zakansis (1998).

(iv) Other Difficulties in Huntington's Disease

Language

The language deficits measured in HD patients may also reflect retained verbal recognition memory coupled with impaired ability to search for and retrieve memories (recall). The ability to name objects (word recognition) is retained until it can no longer be tested because of severe dysarthria or mutism. Similarly, straightforward declaritive speech can be comprehended (or recognised) by HD patients, long after they become mute. However the fluency of expressive language (or recall of words from memory) is severely affected early in the disease process.

In the FAS test of verbal fluency or word recall (Borkowski, Benton, & Spreen 1967), the patient is asked to say as many words as possible that begin with these letters. Quite early in the illness, HD patients score well below education, sex, and age-based norms. Poor performance on the FAS recall test is in sharp contrast to performance on the Boston Naming Test which is a test of picture recognition (BNT-Kaplan, Goodglass, & Weintraub, 1983). The BNT consists of a series of line drawings of common objects that patients are asked to name. Most HD patients usually achieve high scores, even in the advanced stages of illness, if points are not deducted for slow performance (Butters, Sax, Montgomery, & Tarlow, 1978).

Visuospatial ability

Although patients usually do not have apraxia (as measured by their ability to dress themselves or mimic motor acts), their visuospatial skills are clearly abnormal, even early in the illness, when failures cannot be attributed to general cognitive decline or difficulties with motor coordination (Josiassen, Curry, & Mancall 1983). Early deficits have been documented in WAIS subtests measuring visuomotor skill, such as object assembly and block design.

HD patients also have difficulty identifying their position in space (Potegal, 1971), and on tasks involving left-right discrimination (Fedio, Cox, Neophytides, Canal-Frederick, & Chase, 1979).

Changing Sets

Families often report that patients become rigid in their behaviour, unable to change easily from one activity to another, or to change their routines. This may be analogous to the great difficulty they have on cognitive tasks requiring a change in set (Josiassen et al., 1983; Fedio et al., 1979).

1. 2. 3 NEUROPATHOLOGY

As early as 1877 neuropathologic studies demonstrated that the clinical symptoms of Huntington's disease were associated with specific brain changes, particularly in the area of the caudate (Meynert, 1877). Structural neuroimaging studies in living patients with HD have also demonstrated reduced basal ganglia volumes (Harris et al., 1992). These neuropathological changes will be further described in the following section.

1. 2. 4 Summary of Huntington's disease and the motor, emotional and cognitive disorders

- Huntington's disease is an autosomal dominant disorder i.e. off-spring of an infected individual have a fifty percent chance of themselves inheriting the disease.
- The specific gene mutation for HD was identified in 1993, which provided a presymptomatic test for HD that has a sensitivity and specificity of virtually 100%.
- The impact of genetic testing has been investigated as increased rates of suicide in affected individuals, has been reported.
- Most of the evidence suggests that psychological adjustment prior to testing rather than the test result itself was more predictive of psychological adjustment after the test.
- Huntington's disease is characterised by the progressive loss of three primary functions: motor control, emotional control and cognitive function.
- The most easily observable motor abnormality in HD is chorea, however it may be absent or overshadowed by other involuntary movements such as tremor and motor restlessness, bradykinesia, or clumsiness of voluntary movements.
- Individuals with HD may present with affective disorders i.e. depression/anxiety; personality change, and psychotic symptomatology.
- In a clinical setting a complaint frequently expressed is that people with HD display poor judgment as well as other changes in personalities and social behaviour.
- A meta-analysis of the neuropsychological findings of research carried out with people with HD indicated that individuals' are most deficient on tests of delayed recall.
- This deficiency is followed by performance on measures of memory acquisition, cognitive flexibility, and abstraction, manual dexterity, attention/concentration, performance skill and finally verbal skill.
- The language deficits are measured in HD patients may reflect retained verbal recognition memory coupled with impaired ability to search for and retrieve memories.
- Deficits in verbal fluency and visuospatial skills are seen early in the disease.
- Individuals with HD also become rigid in their behaviour, unable to change easily from one activity to another.
- Specific brain changes are seen in the area of the caudate and basal ganglia.

1. 3 NEUROPATHOLOGY AND NEUROPSYCHOLOGY IN PRECLINICAL HUNTINGTON'S DISEASE

In the previous section the clinical disorder of Huntington's disease has been described. The diagnosis of HD is made on the basis of the presence of choreic movements and family history. Research has discovered that the clinical symptoms of HD are accompanied by specific brain changes particularly in the area of the caudate. More recent research has focussed on when this striatal atrophy begins and whether it is associated with early changes in neuropsychological functioning. The results of this research will now be discussed.

1. 3. 1 NEUROPATHOLOGY

Huntington's disease is associated with specific brain changes particularly in the area of the caudate including the basal ganglia. However what is not yet known is when this striatal atrophy begins. Early research is conflicting, VonSattel and colleagues reported no discernible neuropathologic abnormalities in 5 patients with clinically diagnosed HD, leading the researchers to conclude that "the anatomical changes lag behind the development of clinical abnormalities," (VonSattel et al., 1985). However neuropathologic evidence of atrophy of the caudate, putamen, and globus pallidus in an asymptomatic individual with a family history of HD has been reported, suggesting that "substantial functional reserves exist within the striatal system where considerable morphological damage does not find expression in clinical symptoms," (Carrasco & Mukherji, 1968). More recently neuroimaging studies have consistently pointed to basal ganglia compromise in pre-clinical HD (Antonini et al., 1996).

Assuming that striatal atrophy is associated with Huntington's disease, it is important to investigate systematically when this atrophy begins. Neuropathologic studies cannot address this question systematically as very few asymptomatic individuals who are at risk for HD come to autopsy. Aylward et al. (1994) demonstrated that MRI volumes of all the basal ganglia structures were smaller in asymptomatic gene carriers than non-carriers, even after controlling for age, total brain volume, and presence of minor neurologic signs. Preliminary data also suggests that the striatum continues to reduce in volume as persons approach the likely time of symptom onset (i.e. diagnosable illness) (Aylward et al., 1996). In comparison the volume reductions of those mild to moderately affected patients revealed, putamen volumes which were approximately 50% of normal at this stage of the disorder (Harris et al., 1992; Aylward et al., 1996).

However despite a finding by of a significant reduction of basal ganglia volume in asymptomatic individuals (Aylward et al., 1994), other researchers found no correlation between the rate of change of the caudate size and glucose metabolism in nine asymptomatic at risk individuals and suggested that metabolic loss and atrophy may develop independently (Grafton et al., 1992). Consistent with this finding, research has demonstrated no significant changes in the ratio of the size of the caudate, in spite of significant caudate hypometabolism (Antonini, et al., 1996). This finding suggests that at least in the pre-symptomatic phase of the disease striatal atrophy is not a major contributor to the reduced striatal function in HD.

Antonini et al. (1996) also found that the CAG repeat number and the individuals age were the only two significant predictors of MRI and PET changes when considering all symptomatic and asymptomatic Huntington's disease gene carriers. The finding of a significant association between metabolic and receptor binding

decreases, and size of the Huntington's disease mutation is in keeping with previous genetic studies indicating that the CAG repeat number is the main determinant of Huntington's disease onset and progression (Ashizawa, Wong, Richards, Caskey, & Jankovic, 1994; Garzia-Ruiz et al., 1995). However, the mechanism by which the expansion of the CAG repeats causes the Huntington's disease phenotype are not completely understood. The enlarged CAG repeat is translated into a protein, named Huntingtin, which has been detected in neuronal cell bodies and nerve endings, has unknown function and shows no specific regional distribution (Landwehrmeyer et al., 1995; Trottier et al., 1995). The prominence of neuronal loss in the striatum indicates that striatal projection neurons may have some still unknown characteristics, that make them particularly vulnerable to the Huntington's disease mutation product.

1. 3. 2 NEUROPSYCHOLOGY

Thus as it appears that basal ganglia damage is present pre-clinically in HD, it suggests the possibility that given a sensitive enough cognitive or behavioural marker that preclinial impairments may well be observable. The findings from neuropsychological research will now be described.

Together with genetic analysis and brain anatomical correlations, neuropsychological testing has been performed either on asymptomatic subjects at high risk for Huntington's disease (indirect method) (Jason et al. 1988; Strauss & Brandt, 1990; Diamond et al. 1992) or asymptomatic gene carriers (direct method) (Foroud et al., 1995; Giordani et al., 1995; Blackmore, Simpson, & Crawford, 1995), to assess the presence of early cognitive markers of Huntington's disease. The results of these neuropsychological investigations have been somewhat

inconsistent. For example four of these studies report pre-clinical cognitive impairment in mutation carriers (Foroud et al., 1995; Rosenberg, Sorensen, & Christensen, 1995; Siemers et al., 1996; Gray et al., 1997) on measures of psychomotor speed, memory and emotion recognition, whilst four studies report no differences between, mutation-positive i.e gene carriers and mutation-negative subjects i.e individuals tested who do not have the gene (Blackmore et al., 1995; Campodonico et al., 1996; Gomez-Tortosa, del Bario, Barroso, Garcia Ruiz, 1995; de Boo et al., 1997).

However Hahn-Barma and collegues have highlighted that the numbers of asymptomatic patients were rather small in most studies and the differences were neither robust nor consistently found (Hahn-Barma et al., 1998). These researchers also suggested that one explanation for these inconsistent results may be that in these studies, the group of gene carriers were considered as a whole, which included variable proportions of both at risk subjects with no cognitive impairment (presumably far from developing the disease) and at risk subjects with subtle cognitive impairment (Hahn-Barma et al., 1998).

Attempts have been made to overcome these confounding effects and to obtain a greater consistency of outcome using a variety of different methods. Including: using longitudinal investigations (Giordani et al.,1995); linking the more definitive findings of the relationship between the number of CAG repeats and HD onset and progression with neuropsychological factors (e.g. Jason et al., 1997; Hahn-Barma, et al., 1998); or by examining the relationship between basal ganglia volume and neuropsychological functioning (e.g. Campodonico et al., 1996). Hahn-Barma and colleagues also split the asymptomatic group into those with subtle cognitive impairment and those with no impairment (Hahn-Barma, et al.,1998).

Longitudinal Studies

Giordani et al. (1995) carried out an investigation using a longitudinal design employing multiple comparisons of the same gene carriers and non-carriers over a 4-year longitudinal course. The authors considered that at that time when there was limited and contradictory findings in the studies carried out by Diamond et al., (1992), Jason et al., (1988), and Strauss & Brandt, (1990), that a longitudinal design might provide important information about the neuropsychological variability within and between these two groups of carriers and non-carriers.

The results of the Giordani et al. (1995) study of eight closely matched subjects in four different groups; asymptomatic carriers, asymptomatic non-carriers (i.e. people who have been tested but who do not have the HD gene), normal controls, and Huntington's disease subjects, who completed a battery of neuropsychological tasks revealed that although both asymptomatic groups demonstrated variability on select intellectual subtests relative to normal subjects, they did not differ from each other on the three assessments during a 4-year span. Patients with HD performed more poorly than other groups across a range of neuropsychological measures.

Thus importantly the Giordani et al., (1995) study found that asymptomatic subjects as a group regardless of their HD gene status, tended to perform more poorly on some measures of formal intellectual functioning (although not on other aspects of neuropsychological functioning) than normal controls. This observation has been reported previously (Josiassen et al., 1983; Fedio et al., 1979; Josiassen et al., 1982; Catona Lazzarini, & McCormack, 1985), and may be the basis for the hypothesis that any cognitive impairments noted in asymptomatic carriers may reflect early onset of the prodromal period. The lack of differentiation between the

asymptomatic carriers and the asymptomatic non-carriers the authors argued rules against the notion of a prodromal period of the disease (Giordani et al., 1995).

The relatively lower intellectual power in the overall asymptomatic group may instead be related to other familial and environmental factors. For example people are often in the midst of responsibilities of parenthood when HD symptoms are first clearly manifested and diagnosed. Their normal role within the family unit can become adversely affected, not only because of emotional lability and in extreme cases problems with judgement and personality (Folstein et al., 1983). Such disturbances place a high stress level on the family unit. Typically high rates of major affective disorder and other problem behaviours have been reported in children exposed to such family turmoil and disorganisation (Folstein et al., 1983; Robins, 1966; Rutter et al., 1975; Dewhurst, 1970). Early environmental and educational experiences are requisite for adequate intellectual development, even in cases in which such cognitive areas as memory and attention abilities less sensitive to developmental factors, are later found to be adequate.

Although the patient and normal control groups did not differ with regard to age or education, the fact that the controls were likely to have come from an intellectual community of students may have led to some general heightening of their overall IQ. The variability introduced by educational differences may be particularly apparent when studies have small sample sizes. Therefore due to the relatively small number of subjects and resulting limits on statistical power and possibility of sampling fluctuations there are limits on generalising the results of Giordani and collegues investigation (Giordani et al., 1995).

The results do not preclude changes in neuropsychological performance over time, and continued study of the asymptomatic gene carriers is warranted, particularly considering that the average age of the study groups was below mid-30s. Overall the results of the study are consistent with the discontinuity hypothesis of HD, one in which the neuropsychological symptoms of the disease appear at a given time or develop close to the time of clear disease onset (Giordani et al., 1995).

Linking of the number of CAG repeats and neuropsychological functioning

Jason et al., (1997) investigated whether and how the number of repeats affects the clinical presentation of the disease. It has already been demonstrated that higher numbers of CAG repeats are associated with earlier age at onset (Duyao et al., 1993), faster rate of neuronal loss (Furtado et al., 1996), and faster clinical progression (Illarioshkin et al., 1994; Brandt et al., 1996), but not with clinical symptoms at presentation (Andrew et al., 1993). In presymptomatic individuals, higher numbers of CAG repeats have been reported to correlate with measures of intelligence (Fouroud et al. 1995) and motor function, (Siemers et al., 1996). The Jason et al. (1997) study examined the cognitive manifestations of HD with respect to age, clinical onset, progression of cognitive decline, and genetic analyses. They used a case series design with people with HD or at risk for HD.

The results demonstrated that in clinical HD, cognitive impairment correlated with number of years affected but not age at onset. The linear regression had a negative intercept, suggesting impaired cognitive function by time of onset. In the gene carriers, lower cognitive performance correlated with more trinucleotide repeats. In clinical HD trinucleotide repeats interacted with disease chronicity such that the more repeats were associated with worse performance over time; the overall effect was small compared with the effect of the disease chronicity alone. Except for one

carrier, mood state was not associated with cognitive performance in either patients' with HD or gene carriers.

Jason and colleagues concluded that cognitive decline appeared before clinical onset of HD, and is correlated with the number of trinucleotide repeats. Subsequent cognitive decline is primarily a function of years affected, although there is evidence that the presence of more trinucleotide repeats is associated with faster deterioration (Jason et al., 1997).

To avoid this confounding effect of the variability of asymptomatic gene-carriers, Hahn-Barma et al. (1998) performed a three-step analysis of the performance of gene carriers, (1) by comparing gene carriers and non-carriers on a large neuropsychological battery, (2) by looking for correlations between the number of CAG repeats and efficiency on the neuropsychological tests within the group of gene carriers, and (3) by subdividing the group of gene carriers into two subgroups on the basis of their performance on the memory subtests best correlated with CAG repeats. Their underlying hypothesis was that gene carriers with cognitive impairment already have Huntington's disease, despite total lack of motor abnormalities and will develop the full range of symptoms earlier than those without cognitive impairment. The authors stated that if this hypothesis was valid, it should be possible to predict the onset of the disease in the absence of any motor or affective disorder, on the basis of some early modifications of cognitive efficiency, which might constitute sensitive markers.

Ninety-one asymptomatic gene carriers completed the assessments. The results of the study showed significant differences in cognitive performance of non-carriers and gene carriers for Huntington's disease. These differences concern verbal

memory such as logical memory and paired associates subtests of the Wechlser Memory Scale-WMS (Wechsler, 1987) and number of hits and discriminability of recognition at the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987).

By contrast other authors have reported no sign of cognitive impairment, either in subjects at high risk or in gene carriers (i.e. Giordani et al., 1995; Strauss et al., 1985; Rothlind et al., 1993). As highlighted, differences in selected tests may have resulted from the relatively low numbers. However another possible relevant factor, stressed by Jossiassen, Curry, Roemer (1983) (but critically re-examined, by Strauss & Brandt, 1985), is that the variability in performance of subjects at high risk is greater that that of subjects at low risk.

Thus Hahn-Barma et al. (1998) examined the heterogeneity of the group of gene carriers. The correlational analysis indicated that at least for tests of executive function and the hard paired associates subtests of the WMS, such a heterogeneity is related to the number of CAG repeats. Hard pairs are typically much more sensitive to brain damage than easy pairs, because they assess retention of new, unfamiliar associations (which require the initiation of active research strategies in memory), as opposed to automatic recall of well learned verbal associations for easy pairs.

The data from this study indicate that the cognitively impaired carriers significantly differed from both the cognitively unimpaired subgroup and the non-carrier group on a large array of measures, including: most subtests of the WMS (with the notable exception of visual retention); most measures of the CVLT; some tests of executive

functions (arithmetic and digit symbol sub-tests of the WAIS-R, verbal fluency); and global efficiency score on the Mattis Dementia Rating Scale (MDRS- Mattis, 1998)

Therefore it is possible to identify a cognitively impaired subgroup within "asymptomatic" gene carriers. Although these subjects are free of any neurological or psychiatric symptoms, they differ from the normal carriers in neuropathology. It may be that the longer repeat lengths lead to a less circumscribed neuropathology, or that the neurodegenerative process is more advanced. Whether this subgroup will develop the disease earlier, remains to be determined in a follow-up study. However it can be anticipated that the presence of significantly higher CAG repeats in the cognitively impaired gene carriers will be associated with an earlier mean age of onset in this subgroup, which would be strongly consistent with their overall results.

Relationship between Basal Ganglia Volume and Neuropsychological Functioning

In relation to these findings of the dysfunction of the caudate nucleus in metabolic studies, Campodonico et al. (1998) carried out a study to investigate the relationship between basal ganglia volume and neuropsychological functioning. The authors assumed that it might be reasonable to hypothesize that early atrophic changes in the striatum are associated with minor, subclinical alterations in cognitive and motor functioning. Recently, Campodonico et al. (1996) found that healthy mutation carriers who were nearing the likely age of onset of movement disorder showed minor declines in sustained attention and mental speed over a two-year period, although their scores remained within the normal range. However it is unclear whether these declines reflected early neuronal loss of the basal ganglia. Thus Campodonico et al. (1998) investigated whether reductions in caudate and putamen

volume on MRI scans were associated with changes in cognitive and neurologic functioning in 13 healthy adults with the IT-15 mutation.

Similar to the results of other studies, clinically healthy individuals with the HD gene mutation did not as a group differ from those with the normal gene on neuropsychological tests sensitive to early-stage disease. However they did have smaller caudate nuclei and putamens. Furthermore, reduced size of basal ganglia was associated with greater neurologic abnormality, slower mental processing speed, and poorer verbal learning for individuals who inherited the mutation. These findings suggest that subclinical brain anatomic and cognitive changes begin to occur before persons with the expanded triplicate repeat at IT-15 become overtly symptomatic with HD.

The neuropsychological and neurologic correlates of striatal size in healthy mutation carriers parallel those reported in symtomatic HD patients (Starkstein et al, 1988). In the Campidonico et al. (1998) study verbal learning varied as a function of caudate size, while degree of motor abnormality was dependent on putamen size. Among clinically symptomatic patients, Harris et al. (1996) found that both morphologic and cerebral blood flow measures of the putamen, but not the caudate, were related to Quantified Neurological Examination (QNE-Folstein, Jensen, Leigh, & Folstein, 1983) scores. The QNE is a quantified measure, which was carried out by an experienced neuropsychiatrist, or neuropsychiatric nurse, and subjects were judged on the clinical criteria for HD. It was also found that the Mini Mental State Exam (MMSE-Folstein, Folstein, & McHugh, 1975) scores correlated with the extent of caudate atrophy. The caudate nucleus has reciprocal connections with the dorsolateral prefrontal neocortex and few connections to supplementary motor cortes (Delong, Alexander, Miller & Crutcher, 1990). The putamen has anatomical and functional connections to the supplementary motor cortices (Alexander et al.

1986) and appears to be critically involved in movement (Berent et al., 1988; Starkstein, et al., 1992).

One could argue that the participants in these investigations were already clinically ill with HD. The authors concluded that this was unlikely as there weren't any outliers that might have accounted for positive findings; individuals were excluded at the outset if they met even liberal criteria suggestive of early HD and 18 months following the study, none of the participants had been diagnosed.

Although Campodonico et al. (1998) identified very early changes associated with HD, they concluded that it would be premature to use this information for clinical diagnosis without replication. But if cognitive and neuroanatomic changes reliably occur before the symptoms of HD are evident on clinical examination, a set of criteria might be developed for early detection of disease onset. This improved diagnostic sensitivity would allow the testing of new pharmacologic interventions earlier in the disease development, where they are most likely to be effective in forestalling the onset of HD or slowing its progression.

1.3.4 Summary of Neuropsychological and Neuropathological Factors

- There has been a great deal of inconsistency in the neuropsychological investigations of preclinical HD.
- Attempts have been made to overcome this inconsistency using studies with longitudinal design, or by comparing neuropsychological factors with CAG repeats or neuropathological correlates.
- Longitudinal studies suggest that the lowered performance of gene carriers and non- carriers may result from familial circumstances and not a prodromal period of HD. However it may be that the subjects in these studies were too far away from age of onset to identify any decline in function.
- Neuropathological investigations suggest that cognitive performance is related to the reduced size of the structures of the basal ganglia.
- Investigations, which have examined the number of CAG repeats and neuropsychological factors have found a sub-group within the asymptomatic gene carriers who do display neuropsychological deficits.
- The authors argued that this sub-group actually already have HD and predicted that the onset of clinical symptoms in this sub-group will happen prior to the asymptomatic gene-carriers without any cognitive decline.
- The results of their predictions is to be reported in future research publications.
- Therefore it appears that there is some evidence of neuropsychological deficits in a sub-group of asymptomatic gene carriers who are closer to the onset of clinical HD and as has been said already have HD.
- Thus if both neuropsychological deficits and neuropathological decline are apparent prior to the clinical onset of the disease, that any interventions or treatment aimed at delaying decline should be commenced with the onset of these changes.

1. 4 BEHAVIOURAL DISTURBANCE AND SOCIAL JUDGMENT DEFICITS IN HUNTINGTON'S DISEASE

Early studies have reported that the majority of people with HD presented to mental health or general medical settings with personality disturbance or psychiatric problems, prior to manifesting the choreiform movements necessary to obtain a diagnosis of HD (Dewhurst, Oliver, & McNight, 1970). Among the symptoms noted

to occur in HD are impulsivity, erratic behaviour, aggression, irritability, apathy, emotional lability, reduced initiative, depression, anxiety, psychosis, and others (Burns, Folstein, Brandt, Folstein, 1990; Cummings, 1995; Dewhurst et al., 1970; Hulvershorn, Stout, Paulsen, Siemers, 1999; Jacobs & Huber, 1992; Litvan, Paulsen, Mega, & Cummings, 1998; Martin & Gusella, 1986; Mayeux, 1984; Paulsen, et al., 1996). There are also reports of judgement deficits as well as changes in social behaviour (Stout et al., 2001).

Overlap with Behavioural Disturbance following frontal lobe damage.

There have been similarities reported of the behavioural disturbances in HD such as those described, and those observed with damage to the frontal cortex (Cummings, 1993; Jacob & Huber, 1992; Mega & Cummings, 1994). Indeed an anatomical basis for the similar behavioural disturbances which occur in HD and frontal lobe damage has been established. Cummings (1993) and others have suggested that the similarities between behaviour after frontal cortex damage and behaviour after damage to the basal ganglia are due to the connectivity of these anatomic structures within several frontal subcortical circuits.

These circuits have been described in nonhuman primates as projections from the frontal cortex to the caudate nuclei, which then project back to the frontal cortex or near the location of origin for that circuit (Alexander & Crutcher, 1990; Alexander, Crutcher & Delong, 1986; Alexander, Delong & Strick, 1990). Using this model, disruption of circuits via damage to subcortical structures would be sufficient to produce disturbances in the behaviours subserved by that circuit. Thus in HD damage to the basal ganglia may be responsible for creating behavioural disturbance of a frontal type.

1. 4. 1 FRONTAL LOBES AND BEHAVIOURAL DISTURBANCE

The frontal lobes (FL) play a crucial role in human behaviour and some of the most dramatic neurobehavioural syndromes are associated with frontal lobe dysfunction. Regional specialisation within the FL is recognised with injury of; prefrontal convexity, orbitofrontal and medial frontal cortex producing distinctive syndromes (Cummings, 1993). However similar behavioural changes have been observed in patients with lesions in other brain regions, challenging the anatomic specificity of "frontal lobe" syndromes. As mentioned, researchers have described a series of parallel frontal-subcortical circuits that link regions of the frontal lobes to subcortical structures (Alexander et al; 1986; 1990).

These circuits provide an explanation for understanding the similarity of behavioural changes associated with diverse anatomic lesions. A wide range of behavioural alterations, including disorders of executive function, personality change, mood disturbances and obsessive-compulsive disorder can be linked to dysfunction of frontal sub-cortical circuits. Review of circuit studies of degenerative neurologic diseases or informative focal lesions involving circuit structures are then used to demonstrate the value of frontal-subcortical circuits as an interpretive model for understanding human behaviour disorders.

1. 4. 2 FRONTAL-SUBCORTICAL CIRCUITS

Five circuits are currently recognised: a motor circuit, originating in the supplementary motor area, an oculomotor circuit with origins in the frontal eye fields, and three circuits originating from the pre-frontal cortex (dorsolateral prefrontal

cortex, lateral orbital cortex, anterior cingulate cortex), (Alexander & Crutcher, 1990; Alexander et al., 1986, 1990).

The prototypic structure of all circuits is as follows: the origin is in the frontal lobes, the circuit then projects to the striatal structures (caudate, putamen, and ventral striatum). From the striatum the circuit connects to the globus pallidus and substantia nigra. Projections from these two structures connect to specific thalamic nuclei and there is a final link back to the frontal lobes (see Figure 1.), (Cummings, 1993).

Within each of the circuits there are two pathways

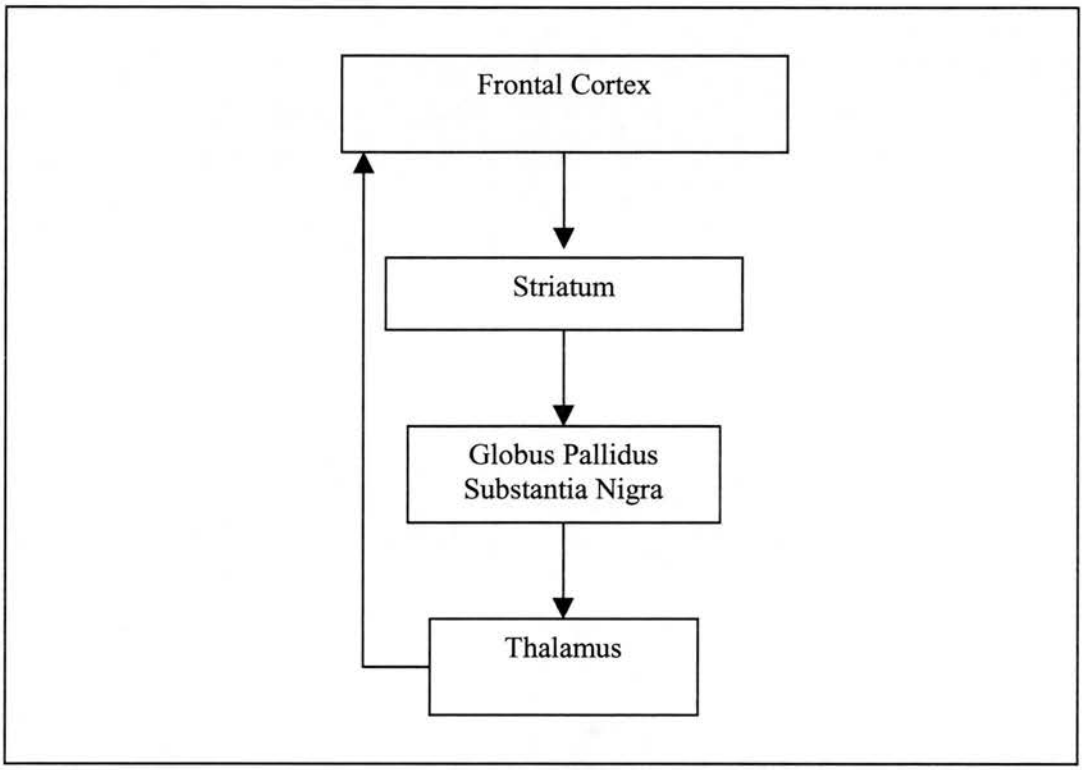
(1) a direct pathway linking the striatum and the globus pallidus interna/substantia nigra complex

(2) an indirect pathway projecting from striatum to globus pallidus externa, then to the subthalamic nucleus, and back to the globus pallidus interna/substantia nigra (Alexander et al., 1990).

Both direct and indirect pathways project to the thalamus. All circuits share common structures but remain anatomically segregated throughout. Projections are progressively focussed onto a smaller number of neurons as they pass from cortical to subcortical structures, but circuit segregation is maintained. There are open and closed aspects to the circuits; structures receive projections from noncircuit cortical areas; thalamus or amygdaloid nuclei and project to regions outside the circuits. Structures projecting onto or receiving projections from specific circuits are anatomically and functionally related (Groenewegen et al., 1990; Parent, 1990). The circuits focus input on restricted cortical targets and several cortical regions project to the striatum, where the output is funnelled through sequential circuit

structures to limited frontal lobe areas (see Cummings, 1993 for further detail of circuits).

Figure 1-General organisation of the frontal-subcortical circuits (Cummings, 1993)



1. 4. 3 FRONTAL-SUBCORTICAL CIRCUIT SYNDROMES

Frontal lobe syndromes.

Three distinct frontal lobe neurobehavioural syndromes are recognised, and each correspond to a region of origin of one of the three prefrontal-subcortical circuits, (See Figure. 2). The dorsolateral prefrontal syndrome is characterised primarily by "executive function" deficits and motor programming abnormalities. Patients with restricted cortical lesions in this area are unable to shift set e.g. WCST. They show reduced verbal and design fluency, poor organisational strategies for learning tasks and poor constructional strategies for copying complex designs (Benton, 1968;

Jones-Gotman, & Milner, 1977). Motor programming disturbances are evident in alternating and reciprocal motor tasks and sequential motor tests (Cummings, 1985). The orbitofrontal syndrome features marked changes in personality (e.g. Logue et al. 1968).

The anterior cingulated syndrome has been studied less extensively. The most dramatic examples of anterior cingulated injury are cases of akinetic mutism associated with bilateral lesions. The patients are profoundly apathetic. Unilateral lesions produce transient akinetic mutism. The major neuropsychological deficit demonstrated in patients with medial frontal lobe lesions is failure at response inhibition on go-no-go tests.

Striatal Syndromes

The dorsolateral prefrontal cortex, projects to the dorsolateral caudate nucleus (see Figure 2.). Mendez and colleagues observed contrasting behavioural consequences of dorsal and ventral caudate lesions. Patients with dorso lesions were more confused and disinterested and those with ventral lesions were disinhibited, euphoric, and inappropriate. These two syndromes recapitulate the corresponding dorsal and ventral frontal lobe syndromes. All patients had deficits on tests of memory, attention, and executive function, including the WCST (Mendez, Adams, Lewandowski, 1989).

Huntington's Disease

HD is the best-known disorder affecting primarily the caudate nuclei. The degeneration begins in the medial caudate region and progresses to affect more lateral areas (VonSattel et al., 1985). Behavioural and neuropsychological abnormalities are marked in HD (e.g. Folstein 1989). There is also evidence of

cognitive impairment in patients wih HD. The deficits manifested are on the WCST, decreased verbal fluency, poor recall of recently learned information, that is, similar to patients with dorsolateral prefrontal dysfunctions.

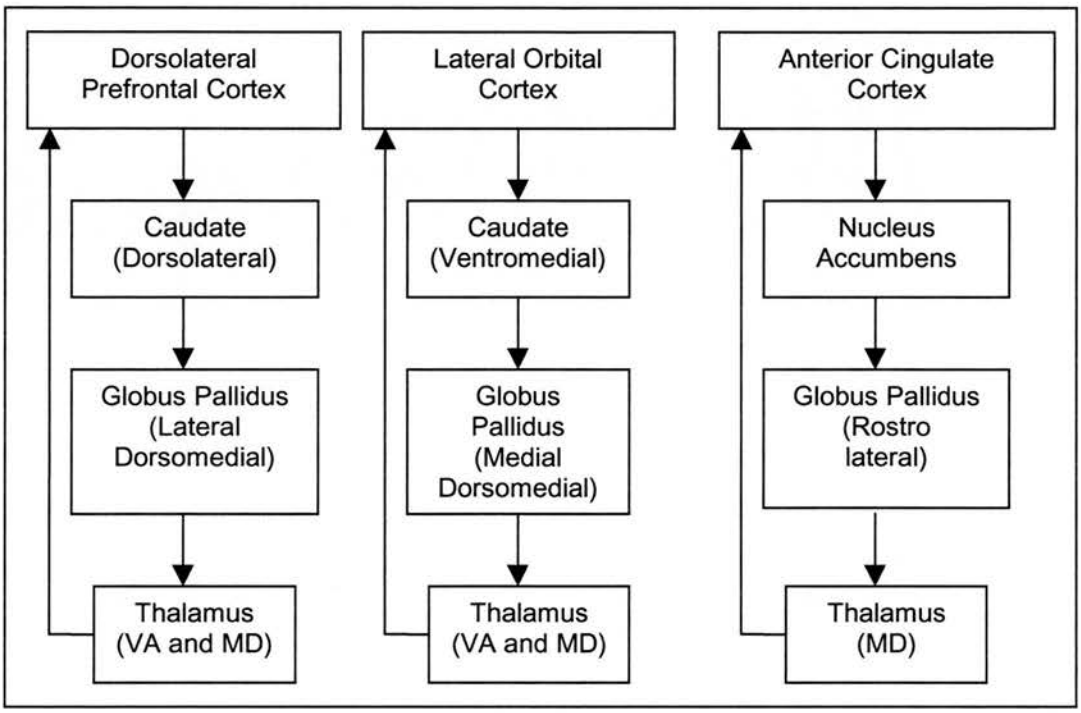
Behavioural abnormalities correlate with the severity of metabolism changes in the caudate and are present when cortical metabolism is normal (Mazziota, 1990). Thus in HD, cognitive and behavioural alterations corresponding to dysfunction of all three behaviourally relevant frontal-caudate circuit projections are evident.

The early appearance of personality alterations in HD corresponds to the involvement of the medial caudate regions receiving projections from the orbitofrontal and anterior cingulated circuits mediating limbic system function. The cognitive deficits of HD reflect involvement of the head of the caudate nucleus receiving lateral prefrontal-striatal projections.

Summary of frontal lobes and behavioural syndromes

Advances in defining the anatomic relationships between the frontal lobes and subcortical structures provide a framework for linking behavioural alterations with frontal subcortical circuit dysfunction. The mode is applicable to neuropsychiatric as well as neurobehavioural disorders and offers insights into the pathophysiology of a variety of human behavioural syndromes. (See Figure 2 for frontal subcortical circuits).

Figure 2. Organisation of the three frontal-subcortical circuits (Cummings, 1993) (VA indicates ventral medial, MD, medial dorsal).



* The indirect circuits and connections of the substantia nigra and the subthalamic nucleus are not shown

1. 4 . 4 MEASURING BEHAVIOURAL DISTURBANCE

The model of frontal-subcortical circuits provides an explanation for the overlap between behavioural disturbances in HD and those observed in people following damage to the frontal lobes. That is, damage to the basal ganglia may be responsible for creating frontal behavioural disturbances in people with HD through disruption of the frontal-subcortical circuits for which the behaviours are subserved. Therefore there is an explanation for the frontal-like behaviours reported in HD, but is the question there a method of quantifying these observed behavioural disturbances. Again, due to overlap in behavioural disturbance in HD and frontal

lobe patients, experimenters have looked to tools used to quantify behavioural disturbance in people with damage to the FL. However there is one main problem with assessing behavioural disturbances in people with frontal lobe damage, in that laboratory-based testing has been insensitive to many of the behavioural disturbances that occur over the course of everyday functioning.

Bechara and collegues have reported a series of studies using a simulated gambling task in the laboratory which they believe may reflect the kind of impulsivity and judgement deficits reported to occur in the daily life in people with FL damage (Bechara et al., 1994; 1996; 1997; 1998; 2000).

Patients with damage to the ventromedial sector of the prefrontal cortices develop severe impairments in real life decision making in spite of otherwise preserved intellect. These impairments are particularly marked in the personal and social realms (Damasio et al., 1990). Bechara et al. (1994) describe an experimental neuropsychology task which simulates in real time, personal real-life decision making relative to the ways it factors uncertainty of premises and outcomes, as well as rewards and punishments. The Bechara et al. (1994) findings indicate that patients with damage to the ventromedial sector of the prefrontal cortices tend to make choices with high immediate reward but severe delayed punishment. The authors suggest a number of reasons for this response pattern concluding that the subjects were unresponsive to future consequences whatever they be and are thus more controlled by immediate prospects.

Bechara et al. (1994) discussed why this 'myopia for the future occurs' stating that there is evidence from other studies that these patients possess and can access the requisite knowledge to conjure up options of actions and scenarios of future

outcomes just as normal controls do (Saver and Damasio, 1991). Their defect seems to be at the level of acting on such knowledge.

1. 4. 5 RISKY DECISION MAKING IN HUNTINGTON'S DISEASE

Because of the similarities reported in the behavioural disturbances in frontal lobe damage and HD, researchers have investigated the performance of people with HD on this simulated gambling task hypothesising that the HD group would demonstrate deficits on this task in comparison to controls. Stout and colleagues reported poorer performance on the simulated gambling task in a group of mildly-to moderately demented research participants with HD (Stout et al., 2001). The findings were similar to those reported by Bechara et al. (1994) in participants with ventromedial frontal lobe damage. In contrast the PD group performed similarly to healthy control group despite having a similar level of cognitive impairment to the HD group. These findings suggest that damage at the subcortical level of the frontal-subcortical brain circuits can produce behavioural changes similar to those observed when damage is located within the frontal cortex itself.

The authors discussed a number of reasons for the poorer performance of HD subjects concluding that poor performance in HD may be more related to problems in learning and concept formation rather than a propensity for risk taking behaviour. They suggested that further studies will be essential for understanding the possible roles of learning, conceptualisation, propensity for risk-taking, or other factors in this simulated gambling task in HD (Stout et al., 2001).

1. 4. 6 SOCIAL JUDGEMENT AND HUNTINGTON'S DISEASE

As already noted, people with HD frequently display poor judgement as well as various other changes in their personalities and social behaviour. However what has not been investigated with people with HD is their judgement relating to social situations. Other frequently quoted problems for people with frontal lobe damage relate to social difficulties. As has been described, there are often parallels drawn between the behavioural disturbances in HD and those observed with damage to the frontal lobes (Cummings, 1993; Jacobs & Huber, 1992; Mega & Cummings, 1994). There is also anatomical basis for these similarities (Cummings, 1993). Thus as there is an anatomical basis and again parallel reports of social difficulties in people with FL damage and HD, that people with HD may demonstrate a similar pattern of deficits in social judgement as do people with FL damage.

1. 4. 7 FRONTAL LOBE DAMAGE AND SOCIAL FUNCTIONING

Patients with damage to the orbito frontal cortex and with ventro medial damage, that is damage which includes both orbital and medial frontal cortex, typically have severe deficits in social functioning (Blumer & Benson, 1975; Damasio et al 1990; Eslinger & Damasio, 1985, etc). These patients are able to correctly analyse social situations in the abstract, but when they respond to similar situations in real life, they choose inappropriate courses of action (Eslinger & Damasio 1985; Saver & Damasio, 1991). These patients often say what the correct response is but have difficulty changing their behaviour to respond appropriately to the social situation or to changing reinforcements in the environment (Rolls, 1996). Orbitofrontal patients often say inappropriate things and appear disinhibited (Mattson & Levin, 1990).

Their conversation typically does not respond to signals of whether the other person is interested in what they are saying or whether they are on topic (Katzmarek, 1984).

There are similarities between OFC patients and patients with autism, as both groups of patients display impaired social judgment, increased indifference, and deficits in the pragmatics of conversation. A frequently quoted deficit in people with autism is problems with Theory of Mind (ToM), which is the ability to infer others' thoughts and feelings. However, little is known about the neurological basis for ToM. It is likely that such a complex cognitive ability, is subserved by a neural network or circuit. Baron-Cohen and Ring (1994) have suggested that due to the similarities in OFC patients and patients with autism that the OFC maybe part of a neural circuit for mind reading, and that the social impairment following OFC damage occurs because part of the Theory of Mind module is damaged.

Recent neuroimaging studies have reported that regions of the frontal lobes appear to be active during TOM tasks, suggesting that these may be part of a TOM circuit. Baron-Cohen et al. (1994) found orbito-frontal activation during a simple TOM task requiring recognition of mental state terms. Fletcher et al. (1995) found activation in Brodmann's area 8 and 9 in the left medial frontal cortex during a more complex ToM task involving deception and belief attribution. Goel, Grafman, Sadato, & Hallet (1995) also found activation in the left medial frontal cortex during a task requiring mental state inferences. However results from lesion patients thus far have not provided any conclusive evidence about which areas might be critical for ToM computations.

Stone, Baron-Cohen & Knight (1998) undertook to test a series of developmentally graded ToM tasks in FL patients to determine if any subtle ToM deficits could be

picked up in patients with lesions in the frontal lobes. They tested patients with damage to the orbito-frontal cortex because they clearly have deficits in social behaviour and because Baron-Cohen et al (1994) found OFC activation with a ToM task. They also tested patients with damage to the dorsolateral frontal cortex to compare their ToM performance to that of the patients tested by Price, Daffner, Stowe, and Mesulam (1990).

The study involved the use of developmentally graded ToM tasks the most complex being the detection of faux pas. Socially normal individuals can usually recognise when someone has committed a faux pas, although specifiying the necessary and sufficient criteria for this is difficult. A working definition of faux pas might be when a speaker says something that the listener might not want to know and which typically has negative consequences that the speaker never intended. The detection of a faux pas is a more advanced theory of mind task because detecting a faux pas requires both an appreciation that there may be a difference between a speaker's knowledge state and that of their listener and an appreciation of the emotional impact of the statement on the listener. Baron-Cohen, O'Riordan, Stone, Jones & Plaisted (1997), developed a faux pas task which was found to be a good measure of subtle ToM deficits.

Stone et al. (1998) found that the performance of bilateral OFC patients on these tasks is parallel to what has been found for individuals with Asperger's syndrome. That is they had no difficulty understanding the stories indexed by their performance on the control questions, but they failed to recognise that some faux pas had been committed. Their performance on this task is consistent with their behaviour in everyday life, in which they frequently say inappropriate things and inappropriately analyse social situations.

1. 4. 8 FRONTOTEMPORAL DEMENTIA AND SOCIAL AND EMOTIONAL DIFFICULTIES

Patients with frontotemporal dementia (FTD) often develop social and emotional difficulties before impairments in cognitive functioning are evident. Families report FTD patients to be uncaring/unaware of others' feelings, and socially inappropriate. To assess if a ToM deficit may underlie these social difficulties, Stone and colleagues tested 13 patients with frontal variant FTD on several ToM tests: false belief, recognition of faux pas and reading of subtle facial expressions. Subjects were also given tests of memory, spatial ability, and executive function. Age-matched controls subjects were given the same tests. Patients were significantly impaired on all ToM tasks relative to controls, and were most impaired on the most developmentally advanced TOM tests (Stone, Gregory, Lough, Baron-Cohen, & Hodges, 2000).

Unlike autism, FTD patients' performance on TOM tasks was not correlated with executive function. These results provide convergent evidence with previous reports for the role of orbitofrontal cortex in social inferences. Theory of mind tests may also be useful in quantifying the social cognitive impairments of patients with FTD, particularly those who still appear normal on standard neuropsychological measures (Stone et al., 2000).

1. 4. 9 SOCIAL INFERENCE DEFICITS AND HUNTINGTON'S DISEASE

As indicated by previous research Huntington's Disease is associated with problems with judgement and decision making (Stout et al., 2001). As described many of the behavioural disturbances evident in HD are similar to the behavioural disturbances in frontal syndromes and an anatomical basis for this similarity has been established (Cummings, 1993). Stout and collegues reported that people with HD displayed impairments in decision-making and judgment on a gambling task (Stout et al., 2001). These findings were consistent with the models of frontal-subcortical brain circuits and behaviour.

As has already been described, similar areas of the brain i.e. the orbitofrontal or ventromedial frontal areas have been associated social/emotional deficits. Thus as similar areas of the brain associated with the frontal-subcortical circuitry are implicated in deficits in social inference it seems feasible that deficits in social inference may also be evident in HD.

As Stone and collegues reported individuals with frontotemporal dementia displayed deficits on tests examining facial expression (Stone et al. 2000). Similarly Sprengelmer et al. (1996), discovered that people with the HD gene who were pre-symtomatic of the disease displayed a particular deficit in their perception of disgust which they concluded had implications for individuals understanding of social situations. As yet there does not appear to be any literature examining impairments in social inference in patients with HD.

1. 5 PRESYMPTOMATIC DEFICITS

As described in the previous section HD is associated with poor judgement as well as changes in personality and social behaviour. Early research reported that the majority of people with HD presented to mental health or general medical settings with personality disturbance prior to the manifestation of choreiform movements, necessary to obtain a diagnosis of HD (Dewhurst et al., 1970). Researchers have recently begun to examine the extent of the problems in judgment and decision making in HD and their association with clinical characteristics (e.g. Stout et al., 2001). However what is yet to be examined is the presence of these judgement deficits in asymptomatic HD gene carriers.

There is substantial evidence of striatal atrophy prior to disease onset in patients with Huntington' disease (see Antonini et al., 1996). There is also a growing body of research suggesting that there are also neuropsychological deficits prior to disease onset which are more evident as the individual approaches disease onset i.e. the appearance of choreiform movements (Hahn-Barma et al., 1998). Thus as there are apparent organic and neuropsychological deficits in asymptomatic individuals with HD then it should perhaps follow that given a sensitive enough behavioural or emotional marker that preclinical impairments may also be observable.

1.4 SUMMARY AND CONCLUSIONS

Huntington's Disease (HD) is an autosomal dominant neurogenerative disorder. It was the first autosomal dominant disorder for which genetic prediction became possible using DNA markers. The genetic marker for Huntington's disease was

localised in 1983 to a DNA marker on chromosome 4 (Gusella et al., 1983). The specific mutation for HD was identified in 1993 (Huntington's Disease Collaborative Research Group, 1993) and it was then recognised that all cases resulted from the same mutational mechanism of trinucleotide repeat expansion. This mutational mechanism provided a presymptomatic test that was highly accurate as it has a specificity and sensitivity of virtually 100%.

Huntington's disease has a characteristic triad of clinical features including dementia, chorea and mood change (Cummings, 1990; Cummings & Benton, 1992 etc). The neuropathological changes that accompany the disease are most marked in the head of the caudate and to a lesser extent, the putamen and globus pallidus (Aylward, et al., 1996). In keeping with the clinical and neuropathological features in HD the syndrome associated with the disease has been noted to include early-onset behavioural changes, and loss of interest, in addition to cognitive changes such as slowing of cognition, impairment of intellectual function, and memory disturbance (Brandt & Butters, 1986; Brandt & Bylsma, 1993; McHugh & Folstein, 1975). This profile constitutes the syndrome of subcortical dementia (Cummings, 1990), and its pattern of deficits has been suggested to reflect dysfunction of frontal-subcortical neuronal circuitry (Cummings, 1993).

Zakzanis (1998) used meta-analytic principles to review the neuropsychological findings in patients with HD. The results indicated that patients with HD are most deficient on tests of delayed recall, followed by performance on measures of memory acquisition, cognitive flexibility and abstraction, manual dexterity, attention/concentration, performance skill and finally verbal skill.

Thus research with individuals' who have clinical HD has indicated that there are both neuropathological and neuropsychological features associated with disease. However the diagnosis of HD is based on the onset of movement disorder, and a family history of the disease, once gene status has been identified. More recently research has focused on when the neuropathological and neuropsychological changes or features start. That is are they apparent prior to the onset of clinical features of the disease?

Brain imaging studies have consistently revealed that the volumes of all basal ganglia structures are smaller in asymptomatic HD gene carriers than non-carriers, and the striatum continues to reduce in volume as persons approach the likely time of symptom onset (i.e. diagnosable illness) (Aylward et al., 1996). However this striatal atrophy has not been found to be a major contributor to the reduced striatal function as measured by MRI and PET changes in HD in the presymptomatic phase of the disease. The main predictor of MRI and PET changes is actually the CAG repeat number, which is the main determinant of HD onset and progression (Ashizawa et al., 1994; Garcia-Ruiz et al., 1995).

The results from neuropsychological investigations have been somewhat inconsistent, however more recent research has suggested that this is due to wide variation in performance of presymptomatic HD participants (Hahn-Barma et al., 1998). Hahn- Barma and colleages actually split their sample of asymptomatic HD gene-carriers into two groups, one with subtle cognitive changes and another with no apparent deficits. The researchers argue that the sub-group with cognitive changes actually already have HD and have predicted that they will develop clinical symptoms prior to the individuals in the other sub-group; the outcome of the prediction is still awaited. Neuropathological investigations, and those which have

examined the number of CAG repeats, have again found sub-groups within the asymptomatic gene carriers who do display cognitive deficits (Campodonico et al., 1998; Jason et al., 1997).

Similarly to their being some evidence of early neuropsychological and neuropathological changes in preclinical HD, reports have suggested that behavioural disturbances including impulsivity, erratic behaviour, aggression, irritability, apathy, emotional lability, reduced initiative, and others exist, prior to the onset of clinical symptomatology (Burns, et al., 1990; Cummings, 1995; Dewhurst et al, 1970; Hulvershorn, et al., 1999; Jacobs & Huber, 1992; Litvan, et al., 1998; Martin & Gusella, 1986; Mayeux, 1984; Paulsen, et al., 1996).

The behavioural disturbances in HD have been paralleled with those observed following damage to the frontal cortex (Cummings, 1993; Jacob & Huber, 1992; Mega & Cummings, 1994). Anatomically this overlap is likely to result from damage to the subcortical structures, which disrupt the series of parallel frontal subcortical circuits that link regions of the frontal lobes to subcortical structures (Alexander et al., 1986; 1990).

Recently Bechara and collegues have used a laboratory based simulated gambling task which they believe may reflect the kind of impulsivity and judgement deficits reported to occur in the daily life in people with Frontal Lobe (FL) damage (Bechara et al., 1994; 1996; 1997; 1998). They used this gambling task to assess decision making deficits in people with damage to the ventromedial sector of the prefrontal cortices, and found deficits in this group of subjects. Stout et al. (2001) used a similar method to assess decision making deficits in people with HD and found a similar pattern of responding in the HD group to those with damage to the prefrontal

cortices. Patients tend to make choices with high immediate reward but severe delayed punishment; Bechara et al. (1994) suggested that this is likely to be due to an unresponsiveness to future consequences.

Stout and colleagues found that subjects' performance on this task was correlated with measures of memory and conceptualisation but not disinhibition. Thus they suggested that people with HD may have had problems learning the win/loss contingencies of the decks and failed to consistently take these into account in their card selection, which may have accounted for the deficits in performance (Stout, et al., 2001).

People with damage to the orbito frontal cortex and ventro medial damage, typically have severe deficits in social functioning (e.g. Blumer & Benson, 1975; Damasio et al., 1990). It has also been reported that people with HD also display deficits in social functioning and social judgement, however the extent of these problems and their association with clinical characteristics have not been assessed. Stone et al. (1998) found that people with bilateral OFC were impaired on a task, which required the detection of faux pas. The detection of faux pas is a subtle Theory of Mind (ToM) task. This is consistent with the finding that regions of the frontal lobes appear to active during ToM tasks, suggesting that these maybe part of a ToM circuit (Baron-Cohen et al., 1994).

It has already been established that the similarities in the behavioural disturbances in people with HD and those with frontal lobe damage can be explained by frontal subcortical circuitry. Thus as people with certain types of frontal lobe damage display deficits on the ToM task requiring the detection of faux pas, that people with HD may also display deficits on the ToM task.

As already highlighted, there are both neuropathological and neuropsychological changes which occur prior to the onset of clinical symptoms. Frequently it is also reported that behavioural disturbances occur prior to symptom onset. Thus it was considered that any deficits in decision making and judgement may also be present preclinically.

CONCLUSION

Recent research has highlighted that people with HD display deficits in decision making (Stout et al., 2001). However these deficits may result from memory defects which have already been highlighted as the main neuropsychological problem in people with clinical HD (Zakzanis, 1998). As only one study has examined decision making deficits in HD subjects, the author considered that the deficits discovered should be further investigated. Also, as there are both neuropsychological and neuropathological changes which occur preclinically, it was considered important to consider if these decision making deficits are also present preclinically. As social judgement deficits have been found in people with frontal lobe damage, and the existence of frontal subcortical circuits have been established, it seems reasonable to predict that people with HD may also display deficits on a complex ToM task. Indeed if deficits in social judgement are apparent in people with clinical HD, it is also important to investigate if these deficits also exist in a preclinial population.

1. 7 AIMS AND HYPOTHESES

This study was carried out to investigate the clinical and preclinical manifestations of Huntington's disease. The problems investigated included judgement and decision making.

Therefore the aims of the study were to investigate:

- Social judgement deficits in people with HD and presymptomatic HD gene carriers using a ToM faux pas task.
- Decision making deficits in people with HD and presymptomatic HD gene carriers using the Iowa-gambling task.
- The association between the number of advantageous deck selections on the gambling task with verbal fluency, semantic fluency, and inhibition of response HD participants and controls. These associations were carried out on an exploratory basis as there is no previous research on which to base a prediction.
- The association between the number of advantageous deck selections on the gambling task and verbal memory in HD participants and controls, as previous research has found a relationship between these two variables in people with HD (Stout et al., 2001).
- The association between risky decision making and social judgement using the gambling task and faux pas task respectively, on the basis of previous findings that damage at the subcortical level of the frontal-subcortical brain circuits can produce behavioural changes similar to those observed when damage is located within the frontal cortex itself and people with damage to the frontal cortex have displayed deficits on both these tasks.

- The association between performance of HD participants and controls on the faux pas task and verbal memory, verbal fluency, semantic fluency and inhibition of response.
- Neuropsychological functioning using a measure of current intellectual functioning, executive function and memory tests.
- The insight of people with HD of their executive functioning difficulties.
- The existence of depression and anxiety in the symptomatic and presymptomatic HD samples.
- The impact of caring for people with HD.

There were two main hypotheses:

(1) That there will be a difference between the groups on the detection of social faux pas.

(2) That there will be a difference between the groups on a measure of risky decision making.

Two additional hypotheses were also investigated:

(3) There will be a positive association between the number of advantageous deck selections in the risky decision task and verbal memory (a) immediate and (b) delayed.

(4) There will be an association between the number of advantageous deck selections in the risky decision task and performance on the faux pas task.

CHAPTER TWO

METHOD

2. 1 DESIGN

The study employed a between subjects group design investigating the performance of three groups of subjects on tasks used to examine risky decision making, and impairments in social judgement. Participants performance on these measures were also correlated with a variety of neuropsychological tests

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2. 2 HUNTINGTON'S DISEASE SUBJECTS

Subjects were recruited from a group of individuals known to the Scottish Huntington's Disease Advisory Service (SHDAS). All individuals in the two experimental groups had undergone DNA analysis at the East of Scotland Clinical Genetics Service at the Western General Hospital in Edinburgh, in order to establish mutation carrier status by means of direct gene testing. Thus the 28 experimental group subjects all had tested positive for the Huntington's disease mutation (36 or more repeats) (Rubinsztein et al, 1996).

At the Genetics Service patients typically undergo a neurological examination to establish symptom status. The clinical diagnosis of Huntington's disease is based on family history and onset of involuntary choreiform movements. Thus if there is no evidence of movement disorder, individuals are said to be presymptomatic disease carriers as it has already been established that have the Huntington's disease mutation. As has already been mentioned the mean age of onset is between 35 to 44 years. Thus the subjects were assigned to one of two groups on the basis of their symptom status: presymptomatic and symptomatic. There were therefore 10 presymptomatic carriers and 14 symptomatic carriers. Participants were excluded if

there was any evidence or history of psychosis, or if it was felt that the assessment process would be too stressful for them. Participants were informed that they could withdraw from the study at anytime.

2. 3 PROCESS OF RECRUITMENT

Once ethical approval had been gained for the study from Fife Health Board Ethics Committee and Lothian Research Ethics Committee, subjects were approached by one of two Huntington's Advisors from the Scottish Huntington's Disease Advisory Service, Marie McGill and Roger Irwin, to ask if they would like to consider taking part in a research project. If individuals expressed an interest they were sent further details about the study and once they had given written informed consent the researcher made an appointment with each subject. (See Appendix 1 for Patient Information Sheets).

2. 4 CONTROL SUBJECTS

Subjects were recruited from members of the general population whom the researcher knew directly or who knew colleagues of the researcher. The participants were within the same age range as the two experimental groups.

Table 1. Summary of Participants Age (mean and standard deviation) and Sex (N)

Group	**Ages (Mean, S.D)**	**Range**	**Sex**	
			Female	Male
Symptomatic	45 (9.85)	23-58	6	8
Asymptomatic	39.4 (6.98)	26-49	4	6
Control	40.54 (12.24)	23-59	3	10

2. 5 PROCEDURE

Once subjects had agreed to take part in the project and had signed the consent form they attended a one and half hour assessment appointment with the researcher. The assessment appointments either took place at the Clinical Genetics Department at the Western General Hospital in Edinburgh; at Glenwood Health Centre, Glenrothes, Fife; Queen Margaret Hospital, Dunfermline; or in the participants homes. Therefore the process of assessment required the researcher to travel extensively.

The assessment involved the completion of a number of measures as detailed below. If possible each participant completed all the assessments within one appointment. If this was not feasible the assessments were completed in two separate appointments.

Subjects in the symptomatic group were asked to give their permission for the researcher to contact an individual who is either involved in their care or who knows them well. Carers were then sent details about the study and asked to complete the questionnaires detailed below.

2. 6 MEASURES

The experimental groups completed two simple psychological tests together with standardised self-report measures of behaviour and affective state. A neuropsychological test battery was also used. Carers of the symptomatic group completed two self-report measures of stress/distress together with a rating of

patient behaviour. The control group completed a similar battery of assessments but the carer measures were not be used.

2. 6. 1 THE MEASUREMENT OF SOCIAL JUDGEMENT

To assess social judgment deficits in people with symptomatic and presymptomatic Huntington's disease participants were asked to complete a Theory of Mind task, which has been used to assess the recognition of faux pas in patients with bilateral OFC (Stone et al., 1998). Research has demonstrated that patients with OFC damage displayed similar deficits to individuals with Asperger's syndrome and patients with fronto temporal dementia (Stone et al., 2000).

Materials

Subjects were presented with 20 stories. They were provided with a copy of the story for them to follow as the researcher read each story. The participants were informed that were to be told some brief stories and then asked some questions about each story. In ten of the stories the subjects were told about the occurrence of a faux pas. There was no memory loading on the task as the page with the story on it was placed in front of each subject while it was being read and while the questions were being asked afterward. The ten stories, which described the occurrence of a faux pas, were combined with ten stories in which no faux pas occurred. The control stories were used to establish that the participants could distinguish between stories in which a faux pas had occurred and those in which no such faux pas occurred.

Example of a faux pas story:

"Jeanette bought her friend Anne a crystal bowl for a wedding gift. Anne had a big wedding and there were a lot of presents to keep track of. About a year later, Jeannete was over one night at Anne's for dinner. Jeannete dropped a wine bottle by accident on the crystal bowl, and the bowl shattered. "I'm really sorry, I've broken the bowl," said Jeanette. "Don't worry," said Anne, "I never liked it anyway. Someone gave it to me for my wedding."

Following each story the participants were asked a series of questions:

(1) Did anyone say anything they shouldn't have said or something inappropriate? (Tests for the detection of faux pas)
(2) Who said something they shouldn't have said? (Tests for the understanding of faux pas)
(3) Why shouldn't they have said it? (Requires understanding of the mental state of listener).
(4) Why did they say it? (Requires understanding of the mental state of the speaker)
(5) How do you think e.g. Jeannete felt? (Tests for empathic understanding of how the person in the story would feel).
(6) An example is, What had Jeanette given Anne for her wedding? (Control question that asks about some detail of the story)

Questions 2 to 5 were only asked if the subject detected the faux pas, that is, answered yes to Question 1. If the subject answered "No" to question 1, the experimenter skipped to Question 6, the control question.

Thus understanding of faux pas requires understanding both a mental state of belief or knowledge and having some empathic understanding of how the person in the story would feel.

In the 10 stories which did not contain a faux pas the participants were asked Question 1 and if they answered "No" (the correct response) they were then asked the control question or questions. If they answered "Yes" to Question 1 (the incorrect response) they scored zero, however they were still asked questions 2 through to 6. (See Appendix 2 for full script of faux pas task).

2. 6. 2 THE MEASUREMENT OF RISKY DECISION MAKING

The Iowa Gambling Task was used to test risky decision making in patients with presymptomatic and symptomatic Huntington's disease. This is a computerised version of the Iowa Gambling Task used previously by Stout and her colleagues to assess risky decision-making in a group of fourteen individuals with Huntington's disease, individuals with Parkinson's disease (PD) and healthy controls. Stout et al. (2001) found that people with Huntington's disease made fewer advantageous selections than the PD or control group. Also in HD, the number of advantageous selections in the gambling task was correlated with measures of memory and conceptualisation but not disinhibition. The authors concluded that people with HD may have had difficulties learning or remembering win/loss contingencies of the decks, or they may have failed to consistently take these into account in their card selections (Stout et al., 2001).

Thus in an attempt to demonstrate that risky decision-making appears prior to symptom onset in individuals with the Huntington's disease gene, and to replicate the impairments highlighted by Stout et al. (2001) all subjects completed this task.

Participants are presented with a lap-top computer and are informed that they are going to complete a gambling task. On the screen the subjects view a green bar

which represents how much money they have won or lost, a red bar which tells the participants how much money they have borrowed and four decks of cards A, B, C, and D.

The participants were informed:

(1) that they start with a loan of $2000 and that this green bar gets bigger or smaller as they win or lose money.
(2) the goal of the task is to maximise profit on the loan of money
(3) that every time they select a card the computer will tell them that they've won some money, it may then tell them that they've lost some money as well.
(2) they are free to switch from one deck to another, at any time, and as often as wished but
(3) they are not told ahead of time how many card selections must be made (the task is stopped after a series of 100 card selections when the words 'Game Over' appear on screen)
(4) that some of the decks are riskier than others so they can win more, or avoid losing if they stay away from the riskier decks.

The rules of winning or losing are not disclosed prior to completing the task, but the player gradually "learns" that two of the decks are "high risk" (A & B) i.e. intermittently produce large rewards but in the long term lead to significant financial losses, whereas two decks (C & D) lead to modest but consistent gains. Healthy individuals have previously been shown to learn to avoid the risky decks, whereas patients with impairments such as medial frontal lobe damage select an excessive number from the risky decks and consequently lose money (Bechara et al, 1994; North & O'Carrol, 2001).

Note: For subjects who were unable to easily manipulate the mouse because of the severity of their movement disorder, the researcher moved and selected the deck of cards once the subjects had chosen.

2. 6. 3 THE MEASUREMENT OF BEHAVIOURAL INSIGHT

Another measure to be employed is the DEX- self-rating and Independent-rating Questionnaire of executive functioning difficulties, from the Behavioural Assessment of the Dysexecutive Syndrome (BADS) (Wilson, Alderman, Burgess, Emslie & Evans, 1996). This assessment tool was used to examine the subjects behavioural insight as it is possible to compare the individual's own ratings of his or her behaviour with a significant others. This measure was looked at with the symptomatic HD group as the majority of the presymptomatic group live independently.

2. 6. 4 THE PRESENCE OF AFFECTIVE DISORDER

The presence of affective disorder was investigated in the symptomatic patient group and their carers and the presymptomatic group using The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). This is a fourteen-item scale developed to provide a brief state measure of both anxiety (seven items) and depression (seven items). Scores of eight to ten on each of the scales have been taken to indicate possible clinical disorder and from 11 to 21 to indicate probable clinical disorder. The internal consistency of the two subscales as assessed by Cronbach's alpha was 0.93 for anxiety and 0.90 for depression (Moorey et al., 1991). The HADS also has good face validity, and concurrent validity (Zigmond & Snaith, 1983). The HADS also has construct validity (Moorey et al., 1991).

2. 6. 5 THE MEASUREMENT OF PERCEIVED STRESS

The Perceived Stress Scale (PSS) was completed by the two experimental groups to measure the levels of stress in individuals who have Huntington's disease and those who are going to develop the disease in some point in their future. The PSS was designed by Cohen, Kamarck and Mermelstein (1983) to measure the 'degree to which situations in one's life are appraised as stressful'. The scale comprises of fourteen items which refer to subjective appraisals of events occurring within a one-month time frame. Scores range from 0 to 56. Higher scores indicate more perceived stress, but no specific categories or cut-offs were suggested by the authors. The mean scores of a stratified random sample of 2,387 people interviewed by telephone (Cohen & Williamson, 1988) for the PSS-14 was 19.62 (S.D 7.49; Range 0-45). The internal consistency of the PSS-14 as assessed by Cronbach's alpha, was 0.84 in the sample tested by Cohen et al. (1983) and 0.75 for the version in Cohen's and Williamson's general population study of 1988.

Since perceived stress is affected both by daily hassles and by the availability of coping resources, you would expect test-retest reliability to be high and over two days the test-retest reliability assessed in college students was 0.85, while over six weeks it was 0.55. Evidence of concurrent validity and predictive validity is limited (see Cohen et al., 1983). However Cohen et al. (1983) found the PSS correlated with indices of depressive symptomatology (0.65 and 0.76).

2. 6. 6 NEUROPSYCHOLOGICAL ASSESSMENT

All participants completed a neuropsychological test battery to assess a number of different factors. This neuropsychological test battery was used to establish that the

groups were comparable. However this is with the realisation that Huntington's disease is characterised by the loss of control over three primary functions including cognitive control. Indeed it is sometimes referred to as a subcortical dementia. It was therefore necessary to have an estimate of premorbid function to establish the comparability of the groups. It was also necessary however to establish individuals' current level of functioning so this was also assessed. The subjects completed a number of standard psychometric tests described below.

2. 6. 6

(i) Pre-morbid Functioning

Years in education was used as a crude measure of pre-morbid function; the NART (Nelson, & Willison, 1991) has not been validated as an accurate measure of pre-morbid abilitity in subcortical dementias.

(ii) Current Level of Functioning

This was assessed using the Wechsler Abbreviated Scale of Intelligence (WASI) (The Psychological Corporation, 1999). The WASI was developed to meet the demands for a short and reliable measure of intelligence in clinical, psychoeducational, and research settings. The WASI is individually administered and is designed for use with individuals aged from 6 to 89 years. The WASI is nationally standardised and yields the three traditional Verbal, Performance, and Full Scale IQ scores. The scale is also linked to the Wechsler intelligence Scale for Children-Third Edition (WISC-III; Wechsler, 1997) and the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III; Wechsler, 1997) and provides tables for estimating IQ score ranges on the WISC-III and the WAIS-III.

The WASI consists of four subtests: Vocabulary, Block Design, Similarities and Matrix Reasoning. These subtests have the highest loading on g or general

intellectual functioning. They were chosen for their strong association with general cognitive abilities (see Brody, 1992; Kamphaus, 1993; Kaufman, 1990; Sattler, 1988; Wechsler, 1991, 1997). Administration of all four subtests is a means of quickly estimating an individual's verbal, non-verbal and general cognitive functioning in approximately 30-40 minutes. Two subtests (Vocabulary and Matrix Reasoning) can be used when time is a major constraint for estimating general cognitive functioning.

With the exception of two symptomatic Huntington's disease subjects who completed two of the subtests, all of the participants completed the four subtests of the WASI. Therefore there is an estimate of all the participants current general intellectual functioning. The reported IQ scores given in the Results sections is based on the two subtests scores WASI-II, so the same measure could be compared across all participants.

(iii) Verbal memory

An estimate of the participants immediate and delayed verbal memory was assessed using the story recall from the Adult Memory and Information Processing Battery (AMIBP- Coughlan & Hollows, 1985). This tool has been externally validated as a measure of verbal memory.

EXECUTIVE FUNCTION TESTS

(iv) Verbal Fluency

Fluency of speech i.e. the speed and ease of verbal production is typically measured by the quantity of words produced, usually within a restricted category or in response to a stimulus and usually within a time limit. In the assessment procedure all the participants completed the Controlled Word Association Test of

letter fluency-FAS (Benton & Hamsher, 1987), in order to assess their verbal fluency. The subjects were asked to generate as many words as possible beginning with the letters F, A and S in that order in 1 minute excluding proper nouns, numbers, and the same word with a different suffix. The score, which is the sum of all acceptable words produced in the three one-minute trials is adjusted for age, sex, and education (Crawford, Moore, & Cameron, 1992). The adjusted scores can then be converted to percentiles. This tool has been used extensively with a number of different populations, including people with Huntington's disease, both symptomatic and asymptomatic individuals.

(v) Category Fluency

As Estes (1974) suggested, word fluency tests provide an excellent means of finding out whether and how well subjects organise their thinking. Fluency tests requiring word generation according to an initial letter give the greatest scope to subjects seeking a strategy for guiding the search for words and are most difficult for subjects who cannot develop strategies of their own. Fluency tests calling for items in a category for example animals which provides structure lacking in those asking for words with an initial letter. Category fluency was therefore assessed using a semantic fluency test (Hodges et al 1992), in which subjects generated the names of as many animals as possible in 60 seconds.

Previous research has demonstrated that letter fluency and semantic fluency are very sensitive to early dementia (Cerhan, Tranel & Jones, 1994; Eslinger, Damasio, Benton, & Van Allen, 1985). However LF and SF have been used to differentiate Alzheimer's disease from disorders such as Huntington's disease presuming that SF would be worse that LF in the AD groups. Recent research has demonstrated a similar pattern of deficits in both AD and HD groups (Suhr & Jones, 1998). However

on a cued version of the tasks HD patients performance had improved significantly. This improvement in cued recall was not investigated here although semantic fluency was measured in each of the three groups.

(vi) Inhibition of Response

The Stroop Colour and Word Test (Stroop, 1935; Golden, 1978; Trenerry, Crosson, DeBoe, & Leber, 1989) which assesses response inhibition, was completed by 35 participants (2 subjects were colour blind). In this task subjects are required to inhibit overlearned responses. Again the mutation-positive i.e. gene carriers in the Lawrence et al. (1998) study demonstrated deficits in inhibitory control mechanisms which is why this measure was used. This assessment is widely validated.

2. 7 ANALYSIS OF THE DATA

2. 7. 1 DATA ANALYSIS

The data was analysed using variety of different statistical tools on the Statistical Package for the Social Sciences (SPSS) Version 9. As the study was designed to examine the differences between three groups of subjects on a series of different measures, various ANOVA techniques including, one-way ANOVA, were used. Non-parametric assessment tools were also used. Spearman's rho was used to examine the relationship between different factors.

2. 7. 2 POWER ANALYSIS

Statistical power is defined as the probability of avoiding a Type II error; rejecting the research hypothesis when it is correct, which is more likely when the sample size is

smaller. With regard to the two main hypotheses of the study in order to achieve a level of power of 0.8 using a between subjects group design; alpha level of 0.05, with the size of the samples used, the effect size required is 0.25 (Clark-Carter, 1997; Cohen, 1988).

CHAPTER THREE

RESULTS

3.1 EXPLORATION OF THE DATA

Due to the limited number of subjects, Kolmogorov-Smirnov analysis was carried out on each data set to examine normality of distribution, the results are displayed in Tables 2 and 3.

Table 2. Comparison of distribution of the subtest scores with normal distribution using Kolmogorov-Smirnov.

Tests of Normality

		Kolmogorov-Smirnov[a]		
	Group	Statistic	df	Sig.
WASI- IQ2	1.00 symptomatic	.137	14	.200*
	2.00 presymptomatic	.180	10	.200*
	3.00 control	.130	13	.200*
Sem. Fluency	1.00 symptomatic	.224	14	.056
	2.00 presymptomatic	.139	10	.200*
	3.00 control	.157	13	.200*
Letter	1.00 symptomatic	.152	14	.200*
	2.00 presymptomatic	.152	10	.200*
	3.00 control	.159	13	.200*
Story Recall Imm.	1.00 symptomatic	.119	14	.200*
	2.00 presymptomatic	.150	10	.200*
	3.00 control	.097	13	.200*
Story Recall Del.	1.00 symptomatic	.167	14	.200*
	2.00 presymptomatic	.179	10	.200*
	3.00 control	.151	13	.200*
Sum C & D	1.00 symptomatic	.146	14	.200*
	2.00 presymptomatic	.168	10	.200*
	3.00 control	.148	13	.200*
NET	1.00 symptomatic	.169	14	.200*
	2.00 presymptomatic	.133	10	.200*
	3.00 control	.144	13	.200*

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

The test of normality on the Stroop and the results from the Faux pas task were carried out independently as not all subjects completed these subtests.

Table 3. Comparison of the distribution of scores on the Stroop and Faux Pas task using Kolmogorov-Smirnov.

	Group	Kolmogorov-Smirnov		
		Statistic	df	Significance
Stroop	1 Symptomatic HD	0.154	12	0.2
	2 Presymptomatic HD	0.314	10	0.006
	3 Control	0.278	13	0.007
Faux Pas Task	1 Symptomatic HD	0.169	10	0.2
	2 Presymptomatic	0.167	10	0.2
	3 Control	0.292	13	0.003

Noticeably the performance of the presymptomatic HD group and control groups scores are not evenly distributed and this is likely to be due to ceiling performance in these groups as demonstrated by the box-plots below. Again the performance on the faux pas task is also not normally distributed due a ceiling performance in the control group.

Figure 3. Box Plot of the spread of scores on the Stroop, by the symptomatic HD, presymptomatic HD, and control participants.

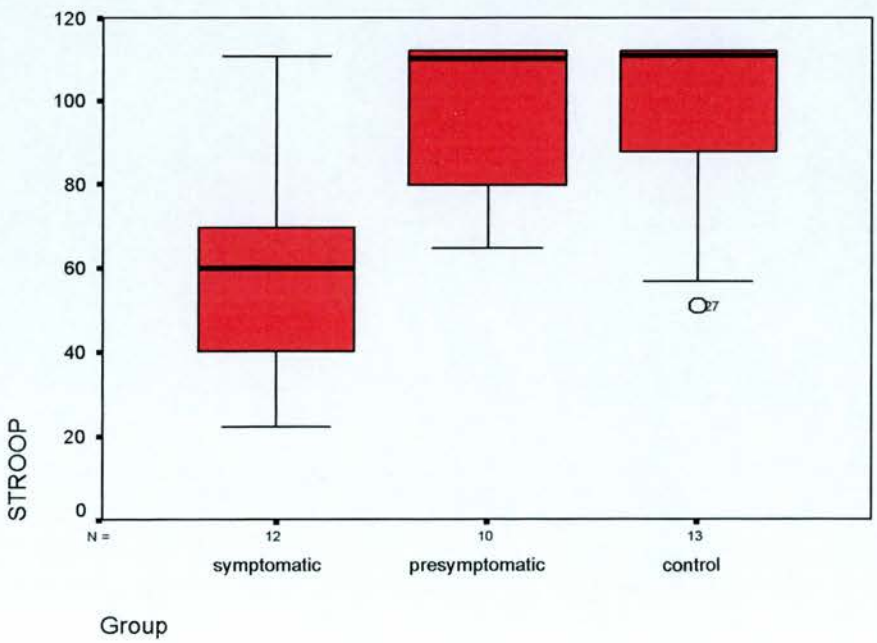
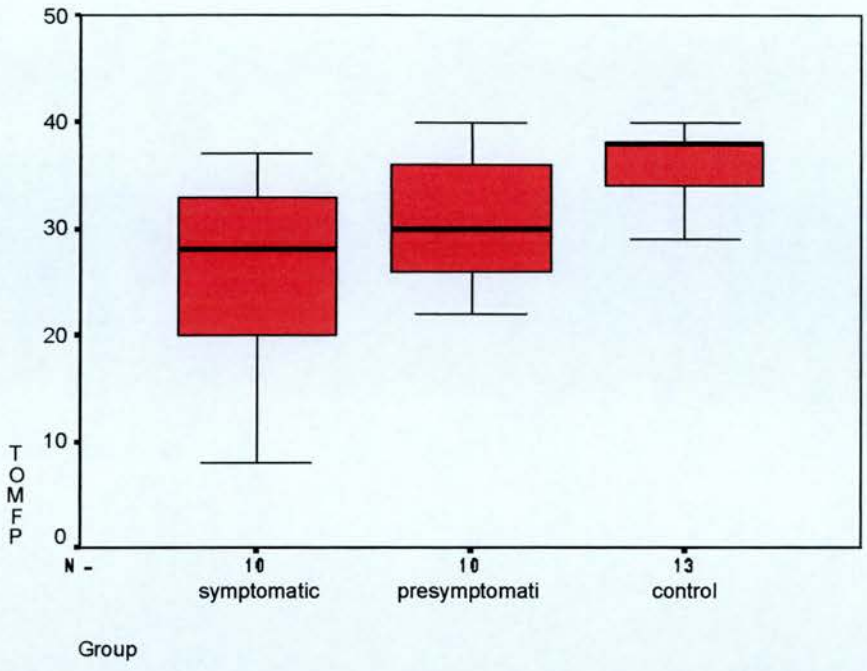


Figure 4. Box plot of the spread of scores on the Faux Pas task by the symptomatic HD, presymptomatic HD, and control participants.



However as the distribution of the majority of the data sets' distribution was not significantly different from a normal distribution the results were analysed using parametric tests in relation to the two main hypotheses. In addition, the results were analysed using non-parametric tests the results of which are given in Appendix 3. In relation to the other two hypotheses the degree of association within each group was analysed using non-parametric statistics due to the small size of the samples.

3. 2 DEMOGRAPHIC DATA

In order to establish that the groups were comparable, demographic data were collected and analysed as displayed below. As noted there were 6 men and 8 women in the symptomatic group, 4 men and 6 women in the presymptomatic group, and 3 men and 10 women in the control group. A cross-tabulation was used to establish if there was a significant difference between the males and females in each group, which revealed no significant difference ($X^2 = 1.3$; $p = 0.522$).

The results of the analysis indicate that the groups are comparable on age (F = 1.082, d.f. = 2, 34, p = 0.35), and years in education (F = 0.277, d.f. = 2, 34, p = 0.76), but there is a statistically significant difference between the IQ's of the groups (F = 5.601, d.f. = 2, 34, p = 0.008). In order to establish where this difference occurred post-hoc analysis was carried out. This revealed that the I.Q of the symptomatic group was significantly different from the presymptomatic group (p < 0.05), and from the control group (p < 0.05) (See Appendix 3 for post hoc tables). This is consistent with the cognitive deterioration in Huntington's disease which will be later discussed.

Table 4: Comparison of symptomatic and presymptomatic Huntington's disease participants and controls on age, education and I.Q (WASI- Full-2) (mean, S.D)

	Symptomatic	Presymptomatic	Control
Age	45 (9.85)	39.4 (6.98)	40.46 (12.31)
Years in Education	11.29 (2.05)	11.6 (1.58)	11.85 (2.12)
I.Q (WASI Full–2)	86.64 (19.39)	101.7 (13.7)	107.92 (16.34)

Note: Because of the significant difference in the groups on the IQ measure, the data sets were analysed controlling for IQ which requires the use of parametric tests. The results of the non-parametric tests are displayed in Appendix 3.

3. 3 HYPOTHESES-RELATED DATA

3. 3. 1 HYPOTHESIS 1: DETECTION OF FAUX PAS

To examine social judgement, the participants completed a Theory of Mind (ToM) task, which examined the detection of a faux pas. The task consisted of a series of 20 stories, 10 of which contained a faux pas and 10 that did not contain a faux pas. Of interest was the ability of the two HD subject groups to detect a faux pas and their responses to a series of faux pas related questions. The task also involved an empathy-related question. Table 5 displays the scores for the subjects on the faux pas related questions and empathy questions.

There is a statistically significant difference between the groups on the responses to the faux pas task (F = 6.618, d.f. = 2, 30, $p < 0.01$, two-tailed) which supports the experimental hypothesis of a between group difference. There were however no between group differences on the empathy question (F = 2.78, d.f. = 2, 30, $p >0.05$). Post-hoc analysis revealed that the difference lies between the symptomatic group and the control group ($p < 0.01$) (See Appendix 3 for post hoc tables). Interestingly there is not a significant difference between the symptomatic group and presymptomatic group ($p > 0.1$). If Figure 4, is examined there is much greater variability in performance in the presymptomatic group than in the control group which has been previously found in presymptomatic gene carriers (Hahn-Barma et al., 1998).

To control for IQ the mean responses to the faux pas related questions were analysed using univariate Anova (F = 3.285, d.f = 2, 30, p = 0.052, two-tailed). In order to control for multiple comparisons, the Bonferroni correction was used and

therefore p is required to be < 0.025 to achieve statistical significance. It could be argued however that a deficit would be predicted in the HD symptomatic group and therefore the hypothesis is actually one-tailed and therefore the *p* value would equal 0.028, which is just outside significance. There was no difference between the groups on the empathy questions when controlling for IQ ($F = 1.167$, d.f. = 2, 30, $p = 0.326$).

Table 5. Comparison of the Huntington's disease patient groups and controls, on detection of Faux pas and empathy (mean, S.D); (*F* and *p* values)

	Faux Pas Questions (1-4)	**Empathy**
Symptomatic	25.8 (10.28)	7.9 (2.42)
Presymptomatic	30.8 (5.77)	9 (1.49)
Control	36.15 (3.34)	9.46 (0.52)
F	6.618	2.78
p	0.004	0.078
***F* (controlling for IQ)**	3.285	1.167
***p* (controlling for IQ)**	0.052	0.326

* Tasks completed by 10 in the symptomatic HD group; 10 presymptomatic &13 controls

As described in the methodology the score on the faux pas stories is based on the subjects' responses to four questions, therefore further examination of the data would reveal where the errors were being made (see Table 6).

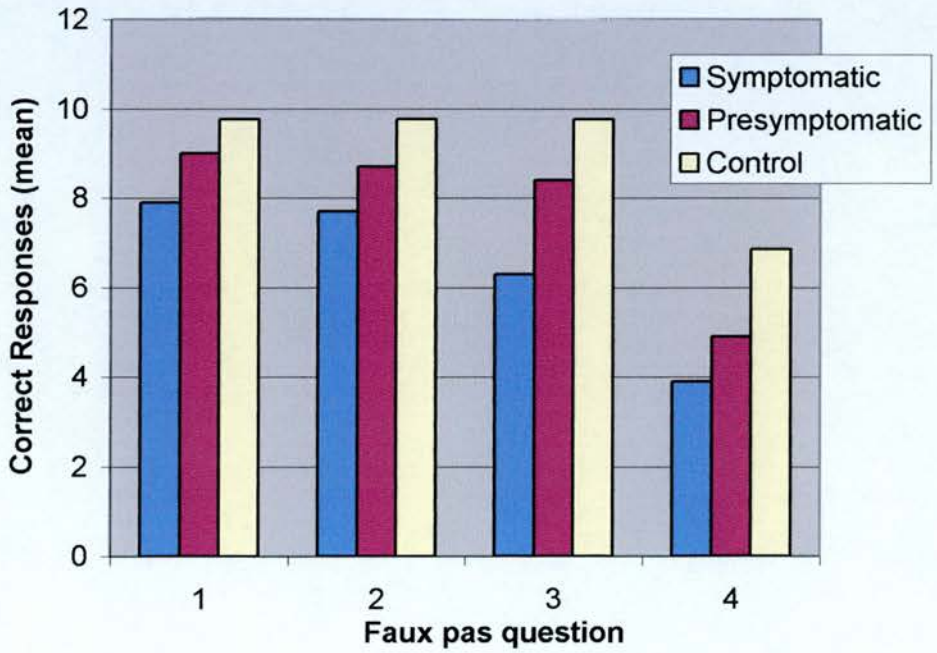
The number of correct responses decreases through the questions 1-4. The pattern of errors is the same for each group, however the control group does display a

greater degree of correct responding in comparison to the two experimental groups. Statistical analysis was carried out on the mean group responses to each question, however as errors due to multiple comparisons may occur the results of the analysis are displayed in Appendix 3.

Table 6. The number of correct responses on the faux pas related questions for the symptomatic and presymptomatic HD participants and controls (mean, S.D.)

Group Tested	Detected Faux Pas	Correctly Named Who Committed Faux Pas	Correct Answer: "Why Shouldn't Have Said?"	Correct Answer: "Why Did They Say It?"
Symptomatic	7.9 (2.42)	7.7 (2.54)	6.3 (3.13)	3.9 (2.73)
Presymptomatic	9 (1.25)	8.7 (1.34)	8.4 (1.96)	4.9 (2.28)
Control	9.77 (0.144)	9.77 (0.44)	9.77 (0.44)	6.85 (2.27)

Figure 5. The number of correct responses on the faux pas related questions for the symptomatic and presymptomatic HD participants and controls



Control Stories

Performance on the stories, which did not contain a faux pas were similar and all groups of subjects were able to identify that a faux pas had not occurred.

Table 7. Comparison of the HD subject groups and controls on the control stories in the Faux Pas task (mean, S.D.).

Control Stories	Symptomatic	Presymptomatic	Control
Identification of No Faux Pas (Max. score = 20)	19.4 (1.9)	19.8 (0.63)	20 (0)
Control Questions (Max. score =21)	20.3 (1.25)	20.7 (0.67)	20.69 (0.48)

3. 3. 2 HYPOTHESIS 2-RISKY DECISION-MAKING

All subjects in the present study completed the Iowa Gambling Game as a measure of risky decision-making. The summary of card selection over 100 trials is shown in Figure 6. There was no effect of group (F = 0.00, d.f. = 2, 34, p = 1.00) a clear affect of card deck (F = 10.732, d.f. = 3, 32, p = 0.000) and critically no group by deck interaction (F = 1.865, d.f. = 6, 66, p = 0.020, two-tailed) i.e. there was not a difference between the groups on deck selection when using multivariate statistics, which does not support the experimental hypothesis. Interestingly however when using univariate tests there was a significant group by deck interaction (F = 2.639, d.f. = 3, 66, p = 0.02). This inconsistency between the multivariate and univariate analyses could result from the variance being high in one of the groups and noticeably the test of Sphericity is just outside significance (X^2 = 10.422, d.f. = 5, p = 0.064). Due to the small size of the sample used one must always be cautious of

interpreting the results of multivariate analyses and on this basis, the results of the univariate analysis are discussed in following section.

When IQ was used as a covariant again there was no effect for group (F=0, d.f. = 2, 34, p = 1), no effect of deck (F= 1.557, d.f. = 3, 32, p = 0.241) and no group by deck effect (F= 1.353, d.f. = 6, 66, p = 0.241) using univariate statistics and similarly there was no effect of deck (F = 2.714, 3,32, p = 0.062) and again no group by deck interaction (F = 1.278, 6, 66, p = 0.280) when using multivariate statistics. With regard to overall financial outcome, all groups lost money and there was no significant between group difference (mean, S.D.), HD-symptomatic = $ 1492 (578. 43) v HD-presymptomatic = $ 1131 (821.57) v control = $114.62 (853.98), ($F$ = 1. 064, d.f..= 2, 34, p = 0.356) (see Figure. 7).

Figure 6. Number of cards selected from each deck by symptomatic and presymptomatic HD participants and controls. (Decks A and B are disadvantageous, C and D are advantageous).

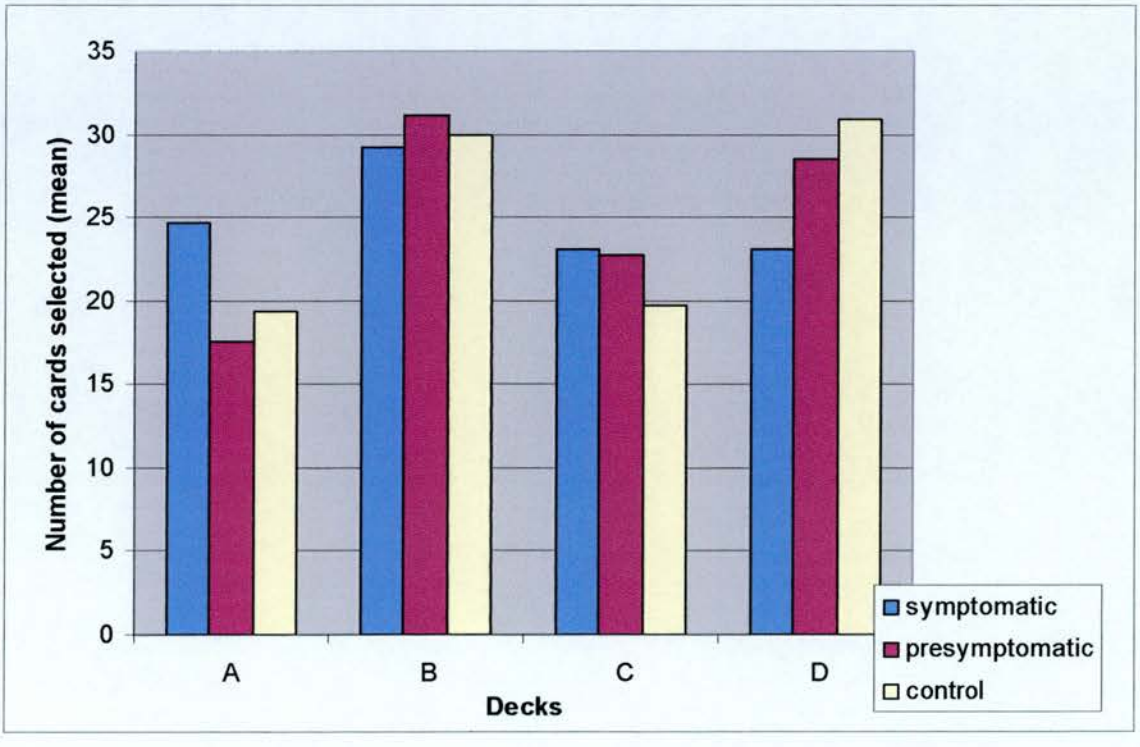
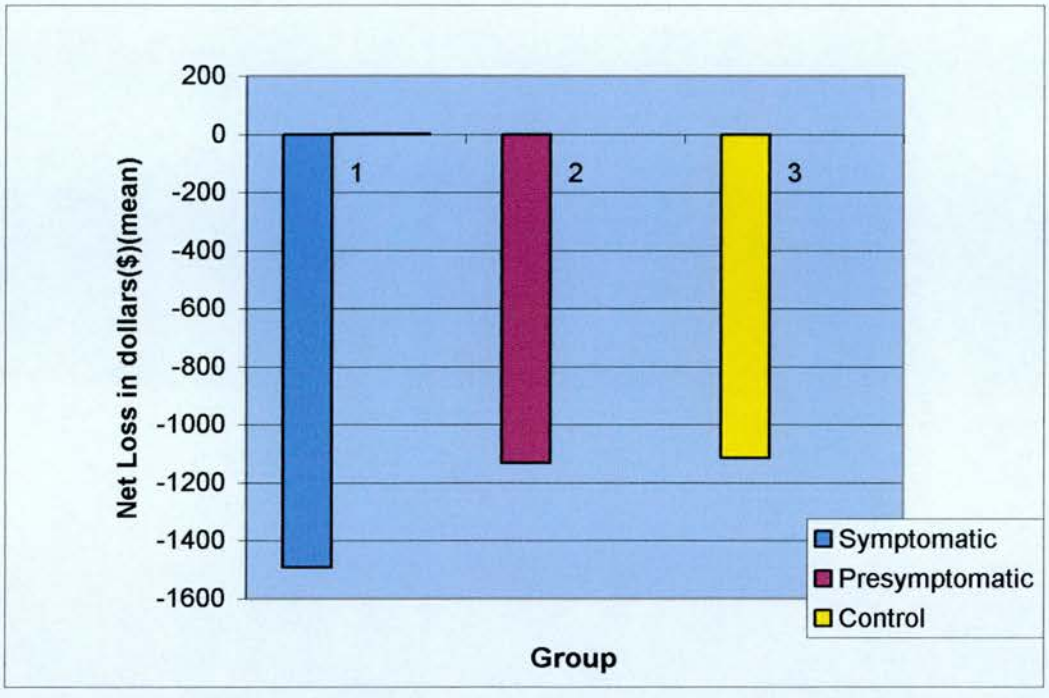


Figure 7. Net financial outcome over a series of 100 trials for symptomatic HD, presymptomatic HD, and control subjects



Learning to Avoid Disadvantageous Decks

The pattern of deck selection gives an indication of the learning of a deck selection strategy i.e. the avoidance of disadvantageous decks. Figures 8, 9 and 10 demonstrate the pattern of deck selection over the 100 selections. Card selections are summed over each block of twenty trials. Figures 9 and 10 demonstrate that there was some evidence of learning in the presymptomatic HD and control participants as there were reduced selections of disadvantageous decks (A & B) by selections 21-40. Figure 8 demonstrates that symptomatic Huntington's disease participants selected from the disadvantageous decks in excess of the advantageous decks (C & D) throughout the 100 trials.

Figure 8. Learning of deck selection strategy over time for symptomatic HD participants.

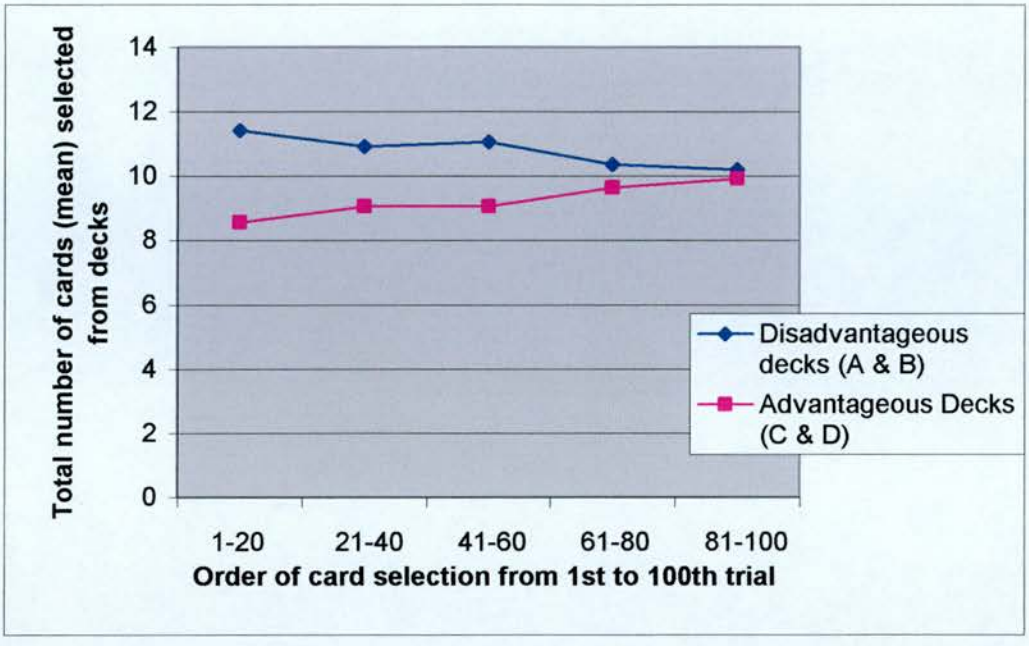


Figure 9. Learning of deck selection strategy over time for presymptomatic HD participants.

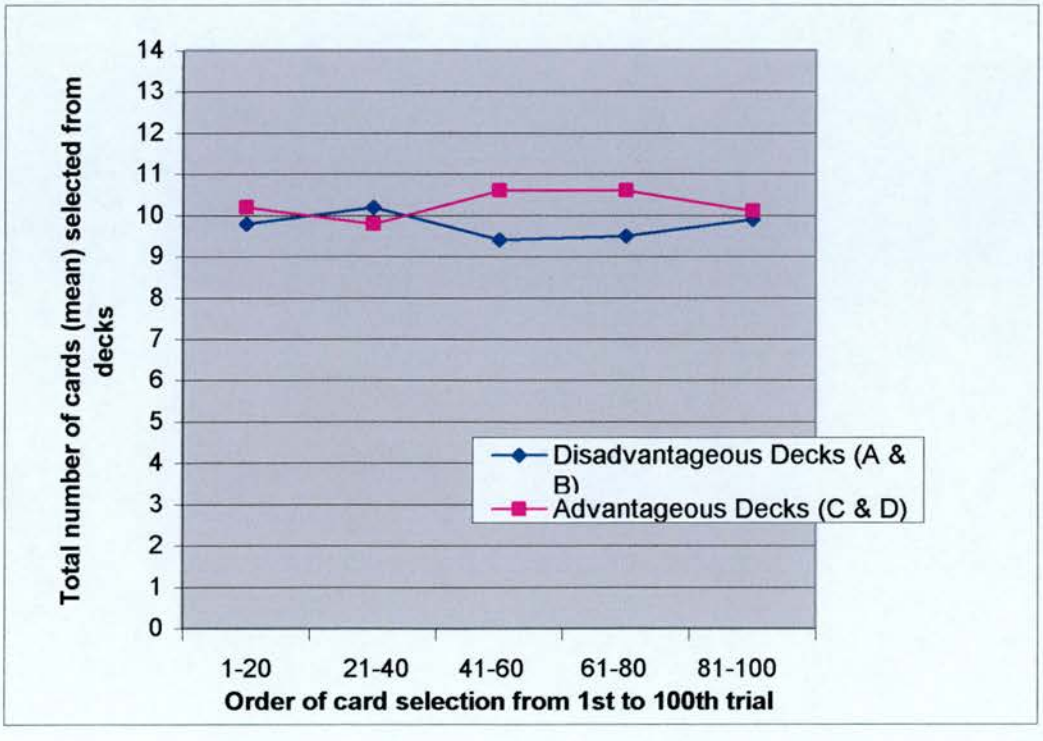
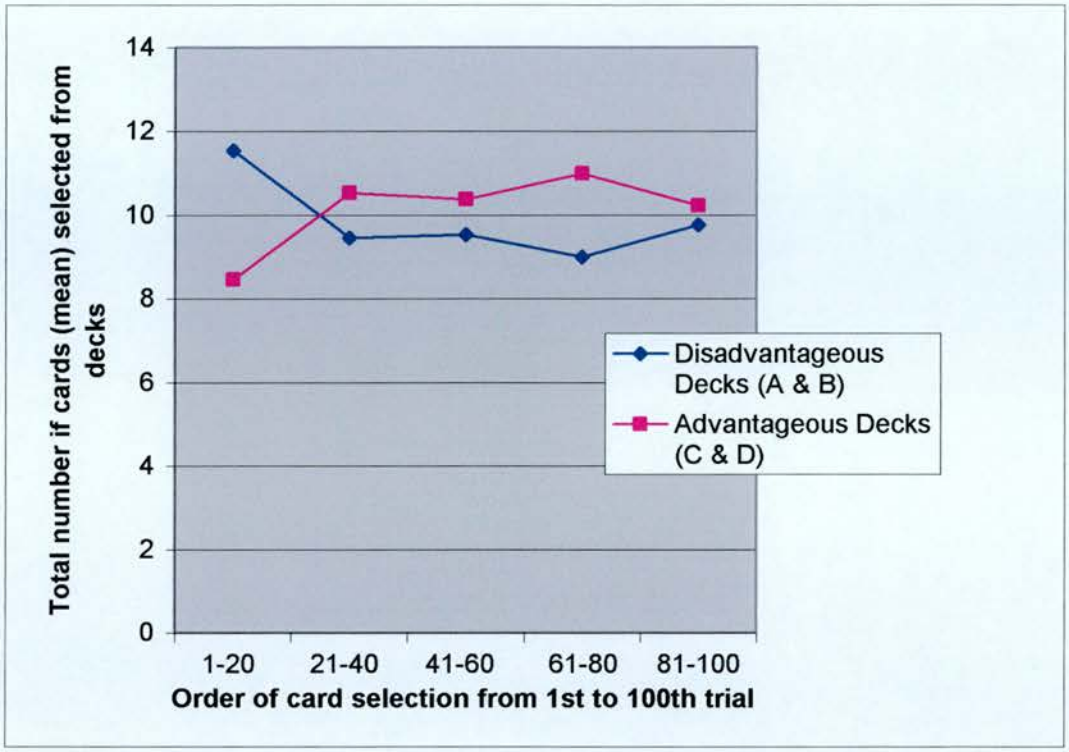


Figure 10. Learning of deck selection strategy over time for healthy control participants



3. 3. 3 HYPOTHESES 3- Association between Advantageous Deck Selection and Verbal Memory (a) Immediate and (b) Delayed.

The level of association between the number of advantageous deck selections in the symptomatic HD group and story recall immediate was (r = 0.457, p = 0.05, one-tailed) and delayed (r = 0.436, p = 0.059, one-tailed). Therefore the findings do appear to support the experimental hypothesis of an association between the number of advantageous decks selected and verbal memory (a) immediate, which is just at significance but not (b) delayed. However as multiple comparisons were being carried out using the Bonferroni correction p must be < 0.0167 to achieve significance. Therefore the experimental hypotheses are not supported, however there does appear to be a relationship between memory and performance on the gambling task which is consistent with Stout and colleagues who found a significant

correlation with the number of advantageous selections and memory (Stout et al., 2001). When analysis was carried using parametric analysis there was an association found between the advantageous selections and verbal memory immediate (r = 0.577, p <0.05), delayed (r = 0.563, p <0.05), and the Stroop (r = 0.588, p <0.05) in the symptomatic HD group. There were no significant associations with letter or semantic fluency $p > 0.1$ (see Appendix 3).

Similarly to comparisons carried out by Stout et al. (2001), in symptomatic HD group, the number of advantageous selections (from decks C & D) summed across selections 61-100 were not significantly correlated with general intellectual functioning as measured by the IQ-2 from the WASI, (r = -0.015, p = 0.958).

There are no other associations with advantageous deck selection in the presymptomatic HD group. There were no associations with advantageous deck selection in any of the measures in the control group.

Pallant (2001) stated that when you are carrying out correlational analysis with an N < 30, it also important to examine variance of scores which is the square of r multiplied by 100, which gives you a measure of predictable variability (see Table 24, Appendix 3). Therefore although there were no significant correlations found between the number of advantageous deck selections and tests of executive function, the variability in performance on the gambling task does predict 25 % of the variability on the Stroop. Also approximately 20 % of the variability in performance on verbal memory (immediate and delayed) in the symptomatic HD group can be predicted from the variability of advantageous deck selections.

Table 8. Correlations of the sum of advantageous selections over decks 61-100 with general level of function, verbal memory and executive functioning.

	Symptomatic HD	Presymptomatic HD	Controls
WASI-IQ 2	-0.015 p = 0.958	0.308 p = 0.386	0.095 p = 0.758
Stroop	0.496 p = 0.101	0.020 p = 0.956	-0.043 p = 0.889
Story Recall Immediate (AMIPB)	0.457 p = 0.05	0.019 0.479	-0.157 p = 0.304
Story Recall Delayed (AMIPB)	0.436 p = 0.059	0.369 p = 0.147	-0.188 p = 0.27
Letter Fluency	-0.01 p = 0.997	0.568 p = 0.087	0.065 0.832
Semantic Fluency	-0.346 p = 0.226	0.032 p = 0.931	-0.130 p = 0.671
Theory of Mind Faux Pas	0.722 p = 0.018	-0.115 p = 0.752	-0.012 p = 0.970

3. 3. 4 HYPOTHESIS 4- Association between advantageous deck selection and score on Theory of Mind Faux Pas Task.

There was an association found between the ranked performance on the Faux Pas task and the number of advantageous selections in symptomatic HD group (r = 0.722, p = 0.018, two-tailed). However the result signifies a trend in association when using the Bonferroni correction p must be < 0.0167 to achieve significance. Therefore the experimental hypothesis is not supported, however the results suggest that if individuals display deficits on the faux pas task they also display deficits on the number of advantageous selections in the gambling task particularly as 52% of the variability in performance on the faux pas task can be explained by the variation in advantageous deck selections.

3. 4 ADDITIONAL FINDINGS

3. 4. 1 Association of performance on the faux pas task and tests of executive function and memory.

The associations of performance on the faux pas task and the performance on tests of executive function and memory for the HD participants and controls, were examined on an exploratory basis. A prediction had not been made on the associations between the faux pas measure and the other sub-tests as there was no research basis for prediction. However interesting associations were found which might warrant further research.

Table 9. Association of performance on the Faux Pas task and measures of Executive Function and Memory (correlation coefficient, *r* and significance level; *p*)

	Symptomatic	Presymptomatic	Control
WASI-2	0.512 $p = 0.130$	0.227 $p = 0.528$	0.842 $p = 0.000$
Stroop	0.762 $p = 0.016$	0.517 $p = 0.126$	0.494 $p = 0.086$
Story Recall (Immediate)	0.750 $p = 0.012$	-0.131 $p = 0.933$	0.652 $p = 0.016$
Story Recall (Delayed)	0.731 $p = 0.016$	0.135 $p = 0.709$	0.749 $p = 0.003$
Letter Fluency	0.158 $p = 0.663$	0.098 $p = 0.787$	0.535 $p = 0.060$
Semantic Fluency	0.059 $p = 0.872$	0.414 $p = 0.235$	0.545 $p = 0.054$

The results displayed in Table 9 suggest that there are associations between performance on the faux pas task with the Stroop ($p < 0.025$); and verbal memory (immediate) ($p < 0.025$) and delayed ($p < 0.025$) in symptomatic HD group. There were no significant associations in the presymptomatic group. However in the

control group there were again associations between the ranked performance on the ToM faux pas task and story recall immediate ($p < 0.01$), delayed ($p < 0.025$) and with IQ, i.e. current level of function ($p < 0.001$). As multiple comparisons were being examined using Bonferroni's correction p must be < 0.0083 for the result to achieve significance. Therefore although there are definite trends in association, the only significant associations exist between the performance of the control group on the faux pas task and story recall (delayed) and current level of functioning.

As mentioned it is important to consider predictable variability (r^2) when examining the relationship between variables. Table 25 in Appendix 3 displays the predictable variability of scores on tests of executive function and memory based on the variation in scores on the faux pas task. The explained variance of performance on the Stroop and story recall (immediate and delayed) is in excess of 50 % based on the variability in performance on the faux pas task in the symptomatic HD group. In the control group the predictable variability is high on each measure particularly IQ suggesting that performance on the faux pas task is highly related to current level of functioning.

3. 4. 2 EXECUTIVE FUNCTIONING NEUROPSYCHOLOGICAL TESTS

As reported a neuropsychological test battery was completed with each of the participants. The interrelationships between these variables were examined. As multiple comparisons were carried out using univariate ANOVA, the Bonferroni correction means that the p value must be at or below $p = 0.0167$ to achieve significance. Therefore the results summarised in the Table 10. indicate that there is significant differences between the groups on all executive function tests Stroop ($p < 0.01$), letter fluency ($p < 0.01$), and semantic fluency ($p < 0.01$).

Table 10- Executive function test results for symptomatic and presymptomatic HD subjects and controls (mean, S.D); d.f = 2.

Group	Stroop	Letter Fluency (corrected)	Semantic Fluency
Symptomatic	57.67 (24.2)	24.57 (9.11)	13.67 (4.7)
Presymptomatic	97.6 (18.44)	39.5 (11.84)	17.4 (7.6)
Control	97.15 (21.56)	23.92 (5.91)	23.92 (5.91)
F Value	13.175	10.589	10.245
p	p = 0.000	p = 0.000	p = 0.000
F (controlling for IQ)	8.757	3.950	4.711
p (controlling for IQ)	p = 0.001	p = 0.029	p = 0.015
d.f. (error)	32	34	34

Post-hoc analysis using Tukey's HSD revealed that differences exist between the symptomatic HD group and the presymptomatic HD group and the symptomatic HD group and controls, on the Stroop, and Letter Fluency. However on the semantic fluency, the symptomatic and presymptomatic HD groups were not significantly different from each other but they were both significantly different from the controls. This is the only task in which the presymptomatic group is different from controls (see Tables 19-21 in Appendix 3).

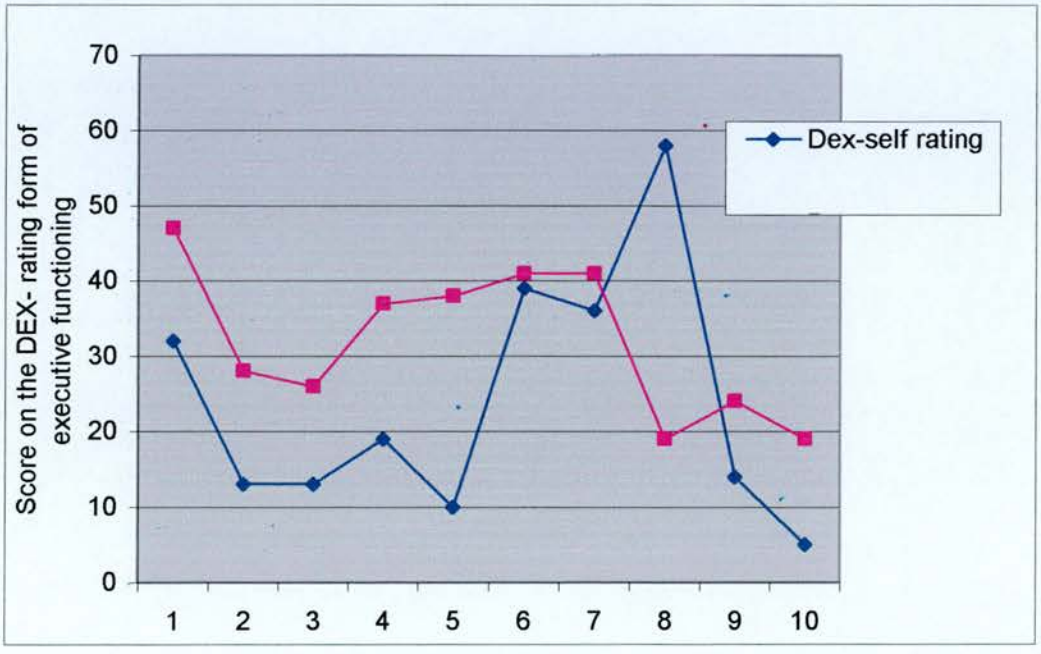
The differences between the performance of the three groups is still significant even when controlling for individuals' current level of functioning i.e. IQ score on WASI-2, on the Stroop ($p < 0.001$); the semantic fluency ($p < 0.0167$); but not letter fluency ($p > 0.0167$). Of note is that the mean score on the Stroop for the HD symptomatic group is below the second percentile and is highly predicative of brain damage. The

results of the executive function tests are consistent with previous research, which will be discussed.

3. 4. 3 SELF AND OTHER RATING OF EXECUTIVE FUNCTIONING DIFFICULTIES

The results of the ratings made by both significant others/ carers and the HD subjects themselves regarding the presence/severity of executive problems using the DEX Questionnaire from the Behavioural Assessment of Dysexecutive Syndrome (BADS) are presented in Figure 11. The mean score and standard deviation (S.D.) for the 10 subjects who completed the task was 23.9 (16.71), and for the independent rater (mean, S.D.) 32, (10.01). This is a useful tool for examining peoples insight about their difficulties. Using non-parametric statistics there is no significant difference between self and others rating (z = 1.667, d.f. = 18, p = 0.096) of behaviour.

Figure 11. Ratings of executive functioning on the DEX- self -rating and DEX-independent rating, for symptomatic HD participants.



* Completed by 10 HD participants and their carers.

If the correlation is examined between self and others ratings of behaviour, the correlation is also not significant ($r = 0.306$, $p = 0.39$).

3. 4. 4 VERBAL MEMORY

All participants completed the story recall (immediate and delayed) from the Adult Memory and Information Processing Battery (AMIPB) as an assessment of verbal memory. The results are displayed in Table 11.

Table 11- Scores on the story recall (immediate and delayed) from the AMIPB for symptomatic and presymptomatic HD subjects and controls (mean, S.D); d.f. = 2, 34

Group	Story Recall (Immediate)	Story Recall (Delayed)
Symptomatic	14.29 (12.13)	11.69 (11.29)
Presymptomatic	31.40 (11.25)	26.40 (12.24)
Control	31.77 (11.03)	29.15 (12.16)
F Value	9.843	8.542
p	0.000	0.001
F Value (Controlling for IQ)	4.032	2.296
p value (Controlling for IQ)	0.027	0.082

There is a significant difference beween the groups on the story recall immediate ($p < 0.001$) and story recall delayed ($p < 0.001$). Post hoc analysis revealed that differences lay between the symptomatic group and the presymptomatic group ($p =$

0.001) and the symptomatic group and controls (p = 0.001) (see Appendix 3 for post-hoc analyses). When controlling for IQ there was no significant difference between the groups on the story recall immediate ($p > 0.025$) or delayed, ($p > 0.025$) (using the Bonferroni correction). This finding suggests that subjects performance on tests of verbal memory are affected by their general level of intellectual functioning as measured by the WASI-IQ-2.

3. 4. 5 CARER STRESS

The incidence of anxiety and depression was examined in the carer population of the symptomatic HD participants using the HADS (Sigmond & Snaith, 1983). Of the 10 who completed the questionnaires 60% had either borderline or clinically significant levels of anxiety and 30% had borderline levels of depression. With regard to the perceived levels of stress on the Perceived Stress Scale (PSS) 20 % had very high levels of stress i.e. 2 standard deviations beyond the mean of a normal population and another 40% had high levels of stress i.e. 1 standard deviation beyond the mean, as measured on the PSS.

3. 4. 6 PRESENCE OF AFFECTIVE DISORDER IN SYMPTOMATIC AND PRESYMPTOMATIC HD SUBJECTS

The incidence of anxiety and depression was examined in the symptomatic HD population again using the HADS. Of the 10 individuals who completed the questionnaires 50% had either borderline or clinically significant levels of anxiety, and 50% had clinically significant levels of depression. With regards to the levels of perceived stress as measured by the PSS, 10% had very high levels of stress (beyond 2 S.D. beyond the mean), and a further 30% had high levels of stress

(beyond 1 S.D. beyond the mean). As there are a number of individuals with significant levels of anxiety and depression any results from the test battery must be interpreted with caution.

In the presymptomatic group six individuals completed the HADS and the PSS and 3 individuals had clinically significant levels of anxiety and one had a score indicative of a depressive disorder (Zigmond & Snaith, 1983). With regards to perceived stress 3 individuals had high levels of stress (beyond 1 S.D. beyond the mean of a 'normal' population).

3. 5 SUMMARY AND CONCLUSIONS

Having established that the majority of scores on the subtests were normally distributed, the decision was made to proceed with parametric statistics. This method of analysis allowed the selection of IQ (as measured on the WASI-2) as a covariate in light of the fact that the IQ of the symptomatic group differed significantly from the mean of the other two groups.

Analysis then proceeded in relation to the two main hypotheses which were that there would be differences in the performances of the groups (symptomatic HD, presymptomatic HD and controls) on the detection of faux task and the Iowa gambling game. Initial analysis supported the main hypothesis, as the performance of the symptomatic group was different from the control group on the faux pas task. Interestingly the performance of the presymptomatic group did not differ significantly from either group, which perhaps warrants further research. On the gambling task there was a significant group by deck interaction reflecting the differences in pattern

of responding over the 100 trials of the task. Figures 8, 9, 10 demonstrate that the symptomatic group did select more disadvantageous decks than advantageous decks throughout the trials, whereas the presymptomatic and control group, gradually learnt to select more advantageous decks.

On the basis of the initial analysis it appears that our hypotheses have been supported. However with subsequent analysis using ANCOVA, which put IQ as a covariate, any significant differences between the groups disappeared. This suggests that the performance on the two tasks investigated reflects individuals' current level of functioning and not premorbid IQ.

The two other hypotheses examined the association between subjects' performance on the gambling task and memory and the association between performance on the gambling task and faux pas task. The results were analysed using nonparametric statistics as the associations within each group scores were examined and due to the small size of the samples this is a more honest reflection of the data. There was an association found between the number of advantageous selections on the gambling task and performance on the faux pas task in the symptomatic group, which was just outside significance and no associations were found with current IQ. There was not a significant association between the number of advantageous selections and verbal memory (immediate and delayed) as hypothesised or with assessments of executive function, when the scores were ranked using the Spearman's rho in each of the groups. However with regard to memory, approximately 20 % of the variance on scores on the memory test (immediate and delayed) was predictable from the variance in performance of the symptomatic HD group on the gambling task. There does therefore appear to be a relationship between performance on the gambling task and memory which is consistent with

previous research e.g. Stout et al. (2000) although the relationship was not significant in this study.

Additional investigations revealed that the performance on the faux pas task was associated with a number of different measures, although there were no hypotheses made for these analyses. The results suggest that there were associations between the performance of the symptomatic group on the faux pas task and verbal memory, indeed in excess of 50 % of the variability in performance on the memory tests (immediate and delayed) is predictable from the variability in performance on the faux pas task. In the control group there were significant associations with delayed verbal memory and current level of functioning i.e. IQ and the explained variance in relation to the faux pas task was in excess of 20 % on all measures and greater that 40 % for verbal memory (immediate and delayed) and over 70% for IQ. Suggesting that performance on the faux pas task is highly related to current level of functioning.

With regard to the neuropsychological test battery there were significant differences between the groups on all tests of executive function.

CHAPTER FOUR

DISCUSSION

4. 1 SUMMARY OF RESEARCH

This study was undertaken to quantify the frequently reported problems with decision making and judgement in people with Huntington's disease (HD). The method employed to assess decision making deficits was the Iowa gambling task which was developed by Bechara and colleagues (Bechara et al., 1994; 1997; 1998; 2000). Prior to the creation of this task there had been difficulties assessing behavioural disturbances in a laboratory-based setting, as the tools had been insensitive to many of the behavioural disturbances that occur over the course of everyday functioning. This simulated gambling task is reported to reflect the kind of impulsivity and judgement deficits that occur in the daily lives of people with frontal lobe damage (Bechara, 1994; 1996; 1997; 1998; 2000). Stout and colleagues used a similar task to assess decision making deficits in people with HD and found that they were impaired on this task relative to people with Parkinson's disease and healthy controls (Stout et al., 2001).

The method employed to detect judgement deficits was a subtle 'Theory of Mind' (ToM) task that involved the detection of faux pas. This task was developed to assess the ToM of children with Asperger's syndrome, as these children are able to solve simpler ToM tasks, despite displaying difficulties in social functioning. Children with Asperger's are impaired in their ability to detect faux pas. Stone et al, (1998) found that the performance of bilateral orbito-frontal cortex patients on these tasks is parallel to what has been found for people with Asperger's syndrome. That is, they had no difficulty understanding the stories indexed by their performance on the control questions, but they failed to recognise that some faux pas had been committed.

As has been highlighted there are often parallels drawn between the behavioural disturbances in HD and those observed with damage to the frontal lobes (Cummings, 1993). These parallels are believed to result from damage at the subcortical level of frontal-subcortical brain circuits, which can produce behavioural changes similar to those observed when damage is located within the frontal cortex itself. There is an anatomical basis for the similarities in behavioural disturbances in people with HD and frontal lobe damage so it seems reasonable to investigate whether deficits in judgement and decision making in HD can be assessed using similar techniques to those used to assess deficits in people with frontal lobe damage i.e. the gambling-task and the task involving the detection of faux pas.

4. 2 DISCUSSION OF THE RESEARCH FINDINGS

4. 2. 1 HYPOTHESIS 1

"There will be a difference between the groups on the detection of social faux pas."

Results of the study indicated that there was a difference between the groups on their performance on the faux pas task which supports the experimental hypothesis. Post- hoc analysis revealed that the only significant differences lay between the symptomatic group and the control group. Therefore it does appear that the symptomatic HD group does display a deficit in social judgement with regard to the ability to detect faux pas. The pattern of deficits on the faux pas task in the symptomatic HD group is similar to patients with bilateral orbito-frontal lobe damage (Stone et al., 1998). The performance of the symptomatic HD group is also consistent with reports made in a clinical setting that people with HD regardless of

their premorbid personalities, display poor judgement as well as various other changes in their personalities and social behaviour (Stout et al., 2001).

However when the analysis was carried with IQ as a covariate, the differences between the groups were not significant ($p = 0.053$). It could be argued however that it was actually predicted that the symptomatic HD group would display a deficit on this task and the hypothesis would therefore be one-tailed which would reduce the p value to $p = 0.028$ which is just outside significance as p must be < 0.025 (using the Bonferroni correction for multiple comparisons) to achieve significance. It does therefore appear that the performance of the HD group is consistent with their current level of function and is not a factor of their premorbid abilities. However one must always be cautious when co-varying IQ as it is a complex measure and social judgement may actually be an aspect of it therefore by co-varying it out you may lose something and increase the likelihood of making a Type 2 error. Further research using an additional control group matched to the symptomatic HD group on IQ would help to clarify if deficits in performance on the faux pas task result from having a lower IQ or if these deficits are specific to the disorder of HD.

As there is not a significant difference between the presymptomatic group and the control group it suggests that the presymptomatic group did not display any deficits on this task. However there is also no difference between the presymptomatic group and the symptomatic group. This is perhaps a reflection of the wide variation in performance of the presymptomatic group. Previous researchers have suggested that the variability in performance of presymptomatic individuals is a factor that has contributed to the inconsistency of research with presymptomatic individuals (Hahn-Barma et al., 1998). That is, studies have shown that presymptomatic HD gene carriers do display premorbid deficits in cognitive function (e.g. Foroud et al., 1995;

Rosenberg et al., 1995), whilst other research has not found such deficits (e.g. Blackmore et al, 1995; Campodonico et al., 1996).

Hahn-Barma et al. (1998) suggested that this variabilty results from being two sub-groups with the presymptomatic population, i.e. those with cognitive deficits and those with no deficits. Hahn-Barma et al. (1998) have actually gone so far as to say that those individuals who are displaying deficits actually already have HD and will develop clinical symptomatology earlier than the subgroup with no impairments. Further research may use a larger sample of presymptomatic individuals and split them into two sub-groups i.e. those with cognitive deficits and those without, to clarify if there is a sub-group within the presymptomatic individuals who do display deficits on the faux pas task.

With regard to the power of the result, a level of 0.88 was achieved. However when the analysis included a control for the subjects' current level of functioning i.e. IQ, the power level fell to 0.565. As the effect size obtained was 0.18, to achieve a power of 0.8 each group would have to contain approximately 17 participants (Clark-Carter, 1997). However it appears that the reduced power is a factor of the subjects' current level of functioning and not a factor of the sample size.

There were no apparent differences between the groups on a measure of empathy, which suggests that the deficits in performance were not a result of a lower level of empathic understanding. However the power of this result is 0.236 and in order to achieve a power of 0.8 with an effect size of 0.074, approximately 30-50 participants would be required for each group.

4. 2. 2 HYPOTHESIS 2

"There will be a difference between the groups on a measure of risky decision making."

Results of the analysis in relation to this hypothesis suggested that although there was no effect of group there was a group by deck interaction. This group by deck interaction suggests that there was a difference between the groups on decks selected i.e. the symptomatic HD group selected more cards from the disadvantageous decks than the presymptomatic and control groups. These results support the experimental hypothesis and are consistent with a study carried out by Stout and colleagues who found that people with HD displayed poorer performance on the simulated gambling task, than people with Parkinson's disease and healthy controls (Stout et al., 2001). These findings are also consistent with previous findings that damage at the subcortical level of the frontal-subcortical brain structures can produce behavioural changes similar to those observed when damage is located within the frontal cortex itself.

The pattern of responding across the 5 blocks of 20 card selections suggests that the control and presymptomatic groups learned to select cards from the more advantageous decks than did the HD participants, particularly towards the end of the 100 trials. Research on decision-making has shown that even when an advantageous pattern of behaviour is established it is common for participants to continue to sample poorer or disadvantageous alternatives (Busemeyer & Myung, 1992; Busemeyer & Townsend, 1993). Consistent with this idea is that individuals in each of the three groups continued to sample from disadvantageous decks throughout the task, particularly deck B. However the findings from the HD group suggests that they did not learn which decks were advantageous or, despite

knowledge of which decks were advantageous, they continued to make frequent selections from disadvantageous decks.

However, when the results were analysed using IQ as a covariate the group by deck effect disappeared i.e. there was no difference between the groups on disadvantageous deck selection. Suggesting that performance of individuals in the symptomatic HD group, (i.e. number of selections from the disadvantageous vs. advantageous decks) was affected by their current level of functioning. Again however as with the faux pas task, when you co-vary IQ you maybe increasing the likelihood of making a Type 2 error as social judgement may be an aspect of IQ. With regard to overall financial outcome all groups lost money and there was no significant between group differences.

The power level of the results of the critical group by deck interaction is 0.84 with an effect size of 0.134. However when IQ was used as a covariate, the power level falls to 0.508 with an effect size of 0.076. Therefore a total sample size of approximately 50 participants would be required to achieve a power of 0.8 with an effect size of 0.076. However it appears that the reduced power of the results of the study is a factor of the current level of functioning of the symptomatic HD group. This is consistent with the results of the Stout et al (2001) study i.e. there appears to be an interaction that is related to current but not premorbid IQ. Stout et al. (2001) used age and years in education as covariates and found that the group by deck interaction remained.

4. 2. 3 Hypothesis 3

"There will be a positive association between the number of advantageous deck selections in the risky decision task with verbal memory (a) immediate and (b) delayed."

Similarly to comparisons carried out by Stout et al. (2001) in symptomatic HD subjects, the number of advantageous selections (from decks C & D) summed across selections 61-100 were not significantly correlated with general intellectual functioning as measured by the IQ-2 from the WASI. Performance in selections 61-100 was also not significantly correlated with memory, which is inconsistent with the research hypothesis.

However when analysis was carried out using a parametric Pearson's correlation there is an association found between the number of advantageous selections and verbal memory (immediate and delayed). Non-parametric statistics are not as powerful as analysis using parametric statistics which increases the likelihood of making a Type-2 error i.e. rejecting the experimental hypothesis when it is correct. Thus it may be a factor of the size of the sample that significance was not achieved and in order to achieve a power of 0.8 would require a sample size of approximately 20-25 participants and this perhaps warrants further research.

Previous research carried out by Stout and colleagues found a correlation with memory measure and a conceptulization measure on the Mattis Dementia Rating Scale (MDRS). The association with recall (immediate and delayed) suggested that memory deficits may underlie the poor performance in the HD participants (Stout et al., 2001). Although the results of the analysis are not significant the variability in performance on the gambling task predicts approximately 20% of the variance in

performance on verbal memory test (immediate and delayed) suggesting memory does account for a fifth of the variability in performance on the faux pas task.

4. 2. 4 Hypothesis 4

"There will be an association between the number of advantageous deck selections in the risky decision task and performance on the faux pas task."

The results of analysis are consistent with the prediction that there would be an association between the number of advantageous deck selections and performance in the faux pas task in the symptomatic HD group. Due to the fact that multiple comparisons were being carried out p must be less than < 0.0167 to achieve significance. Therefore there is a trend of association, but this is not at a sufficient level so as to support the experimental hypothesis. However, 52 % the variability in performance on the faux pas task is predictable from the variability in the number of advantageous deck selections. This is very high level of prediction in the symptomatic HD group and lack of statistical significance of a correlation of $r = 0.72$ is likely to be due to the small size of the sample in the symptomatic HD group. To achieve a power of 0.8 with an $r = 0.722$ would require a sample of approximately 13 participants. However as there a level of predictability between the two measures this is perhaps consistent with the idea that both these tasks utilise frontal-subcortical circuitry.

4. 3 ADDITIONAL FINDINGS

Although there was not an investigated hypothesis relating to the performance of the faux pas (FP) task and other subtests a number of trends in association were discovered. In the symptomatic HD group performance on the FP task was

associated with immediate and delayed story recall which suggests that a memory deficit may underlie the poorer performance in the symptomatic HD group. In the presymptomatic HD group there were however no significant associations found. In the control group there were significant associations found between story recall (immediate and delayed), and performance on the faux pas task also correlated with IQ. The fact that there was an association between memory and performance on the faux pas task is interesting as the test was designed so that it did not involve any memory loading i.e. the subjects each had a copy of the story in front of them. Perhaps this is an area for further investigation.

As all participants completed a neuropsychological test battery the results of the assessments were compared across the three groups. The results revealed that the groups differed significantly on the Stroop, semantic fluency and letter fluency. When IQ was used as a covariate the groups still differed significantly on the Stroop and Semantic Fluency. There were also differences between the groups on immediate and delayed verbal memory and when IQ was used as a covariate the results were just outside significance. The pattern of deficits is consistent with previous research examining cognitive deficits in people with HD (Hahn-Barma et al., 1998)

Post hoc analysis revealed that the performance of the symptomatic HD group differed significantly from the presymptomatic and control group on the Stroop, and letter fluency. However on the category/semantic fluency, the control group differed significantly from both the symptomatic and presymptomatic HD groups who did not differ from each other. This is the only deficit found in the presymptomatic group consistent with previous research that has found deficits in presymptomatic individuals on category fluency (e.g. Lawrence et al. 1998). However this could

again reflect the variability in performance of the presymptomatic group (Hahn-Barma et al. 1998).

The Dex- self and independent rating was used to assess the insight of symptomatic HD participants of their difficulties. It was found that there was no significant difference between the ratings of behavioural difficulties by carers and HD participants. This is inconsistent with the findings of research with frontal lobe patients (Wilson et al., 1996). The ranked correlation was also not significant. However the lack of statistical association may be a factor of sample size and if Figure 11 is examined it demonstrates that patients consistently under rate their behavioural difficulties with the exception of one individual who over rated their behavioural difficulties, both however demonstrate a lack of insight. Consistent findings may have reflected the involvement of the frontal-subcortical circuitry, as a common problem of people with frontal lobe damage is that they under rate their behavioural difficulties (Wilson et al., 1996).

The findings that a substantial proportion of the symptomatic HD group had clinically significant levels of anxiety, depression and high stress levels is perhaps unsurprising given the course and nature of HD. Noticeably half of the presymptomatic sample also had high stress levels and anxiety levels within the clinical range. The results of the study should therefore be interpreted with caution, as anxiety or depression could account for some of the deficits in performance. Also of note is that a substantial proportion of the carers of people with HD also had clinically significant levels of anxiety and depression.

4. 4 EXPLANATIONS FOR RESEARCH FINDINGS

There are a number of explanations for the research findings, which will now be discussed.

4. 4. 1 COGNITIVE DECLINE IN SYMPTOMATIC HD SAMPLE

As it was established when the demographic data of the groups were compared that there was a difference between the groups on a measure of their current level of functioning i.e. IQ. It was considered to be important that this difference was accounted for when any analysis of the results of the study was carried out. Otherwise any significant findings could be discounted by this difference in IQ and any results that remained to be significant when controlling for IQ would prove the test to be highly robust.

As has been discussed, the results of the study in relation to the two main hypothesis of the study were supported in that the symptomatic HD group differed significantly from both the control group and the presymptomatic group on the gambling task and the symptomatic group differed significantly from the control group on the detection of faux pas. When IQ was used as a covariate these differences disappeared which suggests that performance on both these tasks is related to current, but not premorbid IQ i.e. deficits on these tasks are part of the dementia of HD.

There were deficits on the executive function tests, which remained even when IQ was used as a covariate. This suggests that deficits in the inhibition of response and semantic fluency are greater than would be predicted on the basis of an individuals' current level of functioning and are particular to the dementia of HD. Noticeably, the presymptomatic group also differed significantly from the control group on semantic fluency suggesting that this task is sensitive to the subtle cognitive changes in the presymptomatic phase of the illness which is consistent with the results of Lawrence et al. (1998).

4. 4. 2 MEMORY DEFICITS

The Gambling Task

As there were no significant correlations between gambling task performance and performance on the story recall (immediate and delayed) from the AMIPB, it suggests that memory deficits may not underlie the poor performance of HD participants on the gambling task. These results are inconsistent with the results of the Stout study, which found that there was a significant association between the performance of people with HD on gambling task and memory as measured by the MDRS (Stout et al., 2001). However as has been noted the variability in performance on the gambling task is approximately 20 % predictable from the variation in performance on the memory tests and the lack of significant association may be a factor of sample size. The lack of significance was also related to the fact that multiple comparisons were undertaken which changed the significance level.

Stout and colleagues suggested that HD participants might have acted according to the knowledge that the two disadvantageous decks initially offered consistently higher wins than the two advantageous decks. That is, as people were informed of

how much they had won first, followed by how much they had lost. The immediate deck contingencies of higher wins may therefore be more easily remembered than the longer-term selection from a particular deck and overall greater financial outcome long term (Stout et al., 2001).

In the Stout study the deck contingencies were however much more consistent than the contingencies in the computer generated tasks. Two of the decks offered card-by-card wins of $100 while the other two decks offered consistent winning amounts of only $50. The net gain on the last two decks was higher however than the net gain of the first two decks and differential amounts of money were lost.

In this study the deck contingencies were not so consistent in terms of the amount won on each deck and therefore perhaps not so easily learned. However the net gain on the last two decks was consistently greater than on the decks A and B. The initial winnings were much greater on decks A and B prior to loss. The differences in the consistency of deck contingencies may account for the lack of association in this study.

Stout and colleagues suggested that the inability to learn or remember which decks are advantageous may be caused by any of several forms of explicit and implicit learning and memory which are known to be impaired in HD (Brandt & Butters, 1996). For example, given the complexity of the task and the impossibility for participants to recall the precise results of each card selection, participants who perform well in the task may rely on some form of implicit learning to guide response selection. This is consistent with a report by Bechara et al. (1997) that healthy control research participants selected at higher rates from advantageous decks even before they are able to verbalize which of the decks were advantageous. In

this study the participants may have had to rely more on implicit learning than memory as the deck contingencies were not so consistent.

The Faux Pas Task

As mentioned there was a trend of association between performance on the faux pas task and subtests of verbal memory in the symptomatic HD group, suggesting that memory impairments could account for deficits in performance on this task. This is despite the fact that the task was designed so that there was no memory loading (Stone et al., 1998). Indeed the variability in performance on the faux pas task could predict in excess of 50 % of the variation in performance on the memory tasks. In the control group there was also a significant association between performance on the ToM task and verbal memory suggesting there is a relationship between the factors, as there is for IQ. Over 50 % of the variability in performance on the faux pas task could be predicted by the variability in IQ. Therefore performance on the faux pas task may relate to the extent of dementia in the symptomatic HD group. This association perhaps warrants further investigation.

4. 4. 3 POOR JUDGEMENT

The Gambling Task

In addition to problems with learning and memory, poor task performance in the gambling task may occur because of poor judgement. That is, it may be that the HD participants may have learned the contingencies of deck selection but failed to apply that knowledge. This could occur because of a difficulty in simultaneously considering both short and long term outcomes of the task or because there was a greater attraction to short term outcomes than long-term outcomes. In this task, higher short-term rewards were disadvantageous over the long term, while lower

short-term rewards were advantageous over the long term. Thus the design of this task confounds short-term and long-term outcomes, precluding a direct test of the contribution of rewards and punishments in the short and long-term contexts. Bechara et al. (1994) have suggested that in their ventromedial frontal lobe damaged sample, poor gambling-task performance was due to a disregard of future outcomes (Bechara et al., 1994; 1996; 1997; 1998).

The Faux Pas Task

With regard to the faux pas task, deficits in performance on this task may also reflect judgement deficits. This is consistent with the pattern of errors on the faux pas task. As has been highlighted, errors in performance were not a factor of impaired empathy as the majority of participants recognised that the experience of a faux pas would elicit a negative emotion. However the pattern of errors on the task suggests that although participants recognised that people in the story had said things they shouldn't have said and who those persons were, they failed to identify the actual faux pas and why the person actually said what they said i.e. the responses to questions three and four. That is, the participants in the symptomatic HD actually misinterpreted the stories, which may be what is happening in the day-to-day experience of people with HD. In Stone et al. (1998) study, the OFC participants actually failed to identify that a faux pas had been committed. However although in some cases people did fail to identify that a faux pas had been committed, the majority of errors were made interpreting the motives of the characters in the stories i.e. a judgement deficit.

4. 4. 4 INHIBITION OF RESPONSE DEFICIT

The Gambling Task

There was not a significant correlation between the gambling-task performance and the Stroop, which requires the inhibition of an over-learned response. This lack of association suggests that a deficit in response inhibition does not underlie the poorer performance in the HD participants. However with regard to predictable variability approximately 25 % of the variation in performance on the gambling task is predictable from the performance on the Stroop. Therefore the lack of statistical significance may be a factor of sample size and to achieve a power of 0.8 would require a sample of approximately 19 participants. In relation to the gambling-task an inhibition of response deficit would have resulted in participants acting on impulse, rather than carefully considering the long-term consequences of their selections, which may account for some of the variation in performance. This finding is consistent with the Stout et al. (2001) study, as they found no association between the number of advantageous selections and a behavioural measure of disinhibition on the Frontal Lobe Personality Scale (FLOPS: Grace, Stout, & Malloy, 1999). Stout et al. (2001) did suggest however that it might be useful to use a neuropsychological measure of disinhibition in future research.

The Faux Pas Task

There was a trend of association of performance on the Stroop and performance on the faux pas task, and 58 % of the variability in performance on the faux pas task could be predicted from the variability in performance on the Stroop. The lack of statistical association is again likely to be a factor of sample size. The poorer performance in the HD sample may therefore be related to a deficit in the inhibition of response as individuals may have given their initial response to the story, without

actually considering actual details of the stories. In a previous study, which examined deficits in people with Parkinson's disease it was found that there was a trend in association between performance on ToM tasks and executive function tests (Saltzman, Strauss, Hunter & Archibald, 2000).

4. 5 METHODOLOGICAL PROBLEMS

4. 5. 1 PROBLEMS WITH DESIGN

In relation to the two main hypotheses the study utilised a between subjects group design to compare the performance of symptomatic and presymptomatic HD participants and controls on two measures the gambling task and the faux pas task. The study did have some difficulties with recruitment particularly of the presymptomatic participants who were frequently reluctant to take part, which is why there is a lower number of subjects in this group. This reluctance is likely to be due to a fear of a discovery of impairments which have not previously been detected and hence a diagnosis of HD. This is despite assurances that the assessment procedure was not diagnostic in any sense. However individuals who know they have the HD gene may not want to undergo a process, which they believe will highlight any difficulties. Therefore any future research using presymptomatic participants should be aware of the impact that testing could have on these vulnerable individuals.

4. 5. 2 LACK OF STATISTICAL POWER

Statistical power is defined as the probability of avoiding a Type II error-rejecting the research hypothesis when it is correct, which is more likely when the sample size is small as in the case of this study. However with regard to the statistical power achieved in relation to the two main hypotheses of this study, the power of the detection of faux pas is 0.88 and of the deck by group interaction on the gambling-task is 0.84. Thus the probability of making a Type II error is low.

However the results are confused by the fact that the significance of the results and the power of the results are reduced when IQ (current level of functioning) is used as a covariate. Thus the probability of making a Type II error is greatly increased when controlling for IQ. It is however reasonable to conclude that performance of the symptomatic HD group is consistent with their current level of functioning and not premorbid IQ. Therefore even by increasing the size of the sample, IQ or current level of functioning, will affect individual performance on the tasks investigated.

In relation to the third hypothesis (a) and (b), which examined the association between gambling task performance verbal memory (immediate and delayed), the relationship was not significant between the number of advantageous deck selections and memory when the scores were ranked. However there was an association when using parametric analysis, which compared the actual scores. The use of nonparametric statistics reduces the power and increases the likelihood of making a Type-II error, however this was a more honest representation of the data due to the small sizes of the samples. As has been discussed if the size of the

sample was increased a power of 0.8 could be achieved with approximately 20-25 participants.

In relation to the fourth hypothesis, there was a trend of association between gambling-task performance and performance on the faux pas task. The fact that it was a trend as opposed to being statistically significant is more a factor of the use of multiple comparisons as opposed to power. Indeed the variation in performance on the gambling task predicts over 52 % of the variability in gambling task performance. If the relationship between these two measures was examined the level of association would be highly significant.

4. 5. 3 SMALL SAMPLE SIZE

Although the size of the samples was small they were consistent with the size of samples in other research with people with HD (e.g. Stout et al., 2001). The size of the sample relates to the power of the results of an experiment and with regard to the two main hypotheses, the sample sizes were sufficient. However it may be useful to repeat the experiment with a larger sample size particularly in the presymptomatic HD group. With a larger sample, the presymptomatic gene carriers could be split into two sub-groups, those with subtle cognitive impairment and those with no such impairment. It could then be investigated to see if there is a sub-group within the presymptomatic gene carriers' population who does display subtle cognitive impairments and who are also impaired on the tasks investigated, particularly the faux pas task. Previous researchers e.g. Hahn-Barma et al. (1998) have suggested that this sub-group within the preclinical population who have deficits actually have HD already.

4. 5. 4 SELF-SELECTION BIAS

All of the participants in the study kindly volunteered to take part having been approached by people in the Scottish Huntington's Disease Advisory Service. Therefore we may have a biased sample of subjects. In the introduction it was described that only 10% of people at risk for HD go for genetic testing (Babul et al, 1993), therefore any research carried out with HD populations is biased. This does not mean that research should not be carried out with an HD population. However the fact that a sample may not be representative of the entire HD population should be considered when interpreting the results of research.

4. 5. 5 PROBLEMS WITH THE GAMBLING TASK

One of the main methodological problems with the gambling task is that participants frequently reported that they found the task "boring". Therefore the motivation to complete the task was lowered. Also despite being informed that at the beginning of the task, not to try and figure out what the computer was doing Individuals in all groups mentioned that B gave consistently high payouts interspersed with large losses and attempted to figure out the loss contingency. The irregularity of the loss on deck B was however insufficient to discourage participants from selecting this deck. Deck A, which also gave out high losses was avoided by the presymptomatic and control groups, but not the symptomatic group (See Figure 6- Results).

As mentioned in the methodology the researcher had to assist a number of the people in the symptomatic group with the movement of the mouse for deck selection. The movement disorder in these individuals meant that it was very

difficult for them to control the movement of the mouse. A voice-activated task might be more useful for this group.

4. 5. 6 PROBLEMS WITH THE FAUX PAS TASK

The Faux Pas (FP) task required subjects to follow a series of 20 stories and answer questions following the presentation of each story. Four individuals in the symptomatic group did not complete this task three of whom were unable to do so and one did not attend a follow up appointment to complete the assessment. As soon as the researcher started the first story each of the participants said they didn't understand or couldn't follow the story sufficiently to answer the questions so the task was not completed. One could hypothesise as to why they were unable to complete the task, it may be the result of a lack of concentration, or it may reflect a lack of motivation. The individuals who were unable to complete the task were impaired however on a number of the other subtests. It may not therefore be a suitable task for people with more severe dementia.

If the errors on the FP task are examined although the symptomatic HD group consistently make more errors than the presymptomatic and control groups, the pattern of errors is the same across groups. The greatest incorrect responses are to Question 4- Is Why do you think ***Subject*** said it? A correct response requires the responder to reflect back to the actual faux pas or state that the action had been unintentional. Despite having identified the faux pas people frequently stated that the comments made or actions taken had been intentional i.e. the individual in the story had been unkind. This was a frequent error made in the symptomatic HD group but it was also an error made by the presymptomatic and control groups. In an alternative version of the task they use a revised question e.g. Do you think (for

example) Anne knew that Jeannette had given her the bowl for her wedding? This question is a lot more specific and may result in a greater accuracy of responding; further research with people with HD could use this alternative question. (The stories are given in Appendix 4). However as already discussed deficits on this task may reflect judgement deficits based on misinterpretation.

4. 5. 7 EXPERIMENTER BIAS

The researcher was involved with all the assessments; therefore any biasing effects would have had a similar impact on each of the groups. Researchers who have previously investigated the presence of presymptomatic deficits in HD gene carriers have in some instances been unaware of the gene status of subjects to control for biasing affects. Typically however this research has compared two groups of individuals who have all had the test for HD and have been assigned to two groups on the basis of their gene status i.e. positive or negative. In this study the comparison groups were symptomatic and presymptomatic HD gene carriers and the presence of clinical symptomatology was observable in the symptomatic HD sample, which could not be controlled for.

4. 5. 8 PRESENCE OF AFFECTIVE DISORDER IN THE SYMPTOMATIC AND SYMPTOMATIC HD GROUP

Previously of the noted 10 individuals who completed the HADS (Zigmond & Snaith, 1983) in the symptomatic HD group 50% had either borderline or clinically significant levels of anxiety and 50% had clinically significant levels of depression. Also three out of the 6 presymptomatc group who completed the HADS had signicant levels of anxiety and one had clinically significant levels of depression. Therefore the results

of the assessments completed should be interpreted with caution as both depression and anxiety are known to have an impact on peoples' performance on standard neuropsychological tests. Further research may exclude people on the basis of the presence of a significant affective disorder. In this study people were excluded prior to entry to the study if they had a history of psychiatric disorder.

4. 6 FURTHER RESEARCH

There are a number of opportunities for future research some of which have already been highlighted. With regard to the faux pas task as this is the first study which has used this task with a HD population, it would be worth replicating the task to investigate if similar results were discovered. The deficits displayed in the symptomatic HD group were not found in the presymptomatic group. However there was a much greater variability in performance in the presymptomatic group. The variability in performance amongst presymptomatic HD gene carriers has led researchers to suggest that this results from there being two sub-groups within a presymptomatic population those with cognitive impairment and those without impairment (Hahn-Barma et al., 1998). Thus further research examining the tasks investigated in this study could compare the performance of two sub-groups within a population of presymptomatic HD gene carriers to determine if those individuals who have cognitive deficits are impaired on the faux pas task and the gambling task.

Deficits in a presymptomatic population have also been found to correlate with the number of CAG repeats (Hahn-Barma et al., 1998; Jason et al., 1997) and with the reduced size of structures of the basal ganglia (Campidonico et al., 1998). Therefore further research could also examine the association with the number of

CAG repeats and caudate volume with performance on the gambling-task and faux pas task.

As there is an association between neuropathology and the performance of people with the HD gene, it may therefore be useful to examine the activation of the different brain structures using PET scans. This perhaps would provide further information on the activation of different areas of the brain when completing the gambling task and the faux pas task. This is particularly interesting given the apparent trend in association between the gambling and faux pas tasks. This association could perhaps reflect that both tasks involve the same frontal-subcortical circuitry which has been given as an explanation for the similarities in behavioural disturbances in frontal lobe patients and people with HD (Cummings, 1993).

Previous research has found that there is a significant association of performance on the gambling task and memory (Stout et al., 2001). The findings of the current study found that the association was not significant when controlling for multiple comparisons when non-parametric analysis was undertaken, though there was an association using parametric statistics. As there is an inconsistency in the results and the likelihood of making a Type 2 error is greater when using nonparametric statistics this warrants further investigation, particularly as similar numbers of subjects were used in this study and the Stout study (Stout et al., 2001).

There was an association found between the performance on the faux pas task and memory in the symptomatic HD group despite the fact that there was no memory loading on this task. However the task was complex and required a great deal of focussed attention so further research could focus on the relationship between these factors on performance on the faux pas task. The performance of subjects on the

faux pas task may be influenced by the use of slightly different methodology i.e. a change in the wording to question 4, which is more direct question and focuses the participant on the important part of the story and thus this may then lead to different findings.

As mentioned in future research it may be useful to use a control group matched for IQ with the symptomatic HD group. With a matched control group it would be possible to clarify if the deficits in social judgement found are specific to the disorder of HD, or if lowered performance on the tasks investigated are a factor of having a lowered IQ. By using a control group matched to the symptomatic HD group analysis could be carried out without using IQ as a covariate.

4. 7 SUMMARY AND CONCLUSIONS

Huntington's disease is a disorder characterised by dementia, movement disorder and emotional disturbances (Cummings, 1990; Cummings & Benson, 1992; Gusella et al., 1983; Huntington, 1872). Previous research has focused on the motor and cognitive changes associated with the disease. However more recently, investigators have begun to examine the behavioural disturbances that also accompany the disease. It is these behavioural disturbances, which commonly cause difficulties for carers of people with HD. Stout et al. (2001) attempted to quantify judgement and decision making deficits in people with HD. This study was carried out to further investigate these deficits in people with HD using assessment tools which have been previously used to quantify decision making and social judgement deficits in people with frontal lobe damage. The overlap or similarities in the behavioural disturbances in people with HD and those with frontal lobe damage

has been explained anatomically. The existence of frontal-subcortical circuits has been used to account for the parallels in the disturbances between FL and HD patients i.e. in HD, damage to the subcortical region results in deficits or changes in behaviour or function sub served by this circuit (Cummings, 1993).

With regard to the neuropathological changes which accompany HD, there is evidence that the volume of the basal ganglia structures declines prior to the onset of HD symptomatology (Alyward et al, 1996). Therefore much research has focused on whether there are cognitive or neuropsychological changes apparent in the presymptomatic phase of the disease. Research has been somewhat inconsistent but Hahn-Barma et al. (1998) have suggested that this inconsistency results from the variability in performance of people in the presymptomatic phase of the illness. These researchers suggest that there is a subgroup of individuals within the presymptomatic patient population who are displaying cognitive deficits and who will go onto develop clinical symptomatology earlier than a subgroup with no apparent cognitive decline. In this study the presymptomatic group was considered as a whole in order to establish if there was any evidence of a quantifiable deficit in judgement and decision making.

The study examined the performance of two groups of HD patients and controls on a decision making gambling-task and a ToM faux pas task in relation to two main hypotheses which suggested that there would be a difference in the groups on their performance on these tasks. The two main hypotheses were supported by the results of this study as there were significant differences between the groups on performance on the faux pas task and there was a group by deck interaction on the gambling task. Post hoc analysis revealed that the differences on the faux pas task lay between the control group and the symptomatic HD group. The performance of

the presymptomatic group did not differ significantly from either the symptomatic group or the control group and thus it could be concluded that there is no evidence of presymptomatic deficits on the tasks examined. However there was a much greater variability in performance in the presymptomatic group. This suggests that it may be worth investigating if the participants who displayed deficits on these tasks also display other cognitive changes. That is, if there is a subgroup within the presymptomatic HD population who do display cognitive and behavioural changes and who actually develop the clinical symptoms of HD earlier (Hahn-Barma et al., 1998).

The differences between the groups disappeared when their current level of function was controlled for, suggesting performance on this task is consistent with their current and not premorbid functioning.

The study also investigated two additional hypotheses relating to the performance on the gambling task and memory and to investigate if there was any relationship between the performance of participants on the gambling task and the faux pas task. There were no statistically significant associations found between performance on the gambling task and memory this may be a factor of sample size and/or multiple comparisons and perhaps warrants further investigation. There was an association between the performance on the faux pas task and the number of advantageous selections in the symptomatic group, although this again was not significant. However as the explained variance between the two measures was in excess of 50 %, the tasks may be sub served by similar frontal-subcortical circuits.

Additional findings of the study suggest that the performance of the participants on the faux pas task was associated with memory deficits. It may therefore be that

memory deficits may underlie the poorer performance of the symptomatic HD group on the faux pas task. This is interesting because this task is not supposed to have any memory loading. Consistent with previous research there were differences in the groups on all tests of executive function and memory (Hahn-Barma et al., 1998)

A number of different interpretations for the obtained results have been explored including that impaired task performance may reflect a decline in memory or reflect peoples' current level of functioning. However it also could be that the differences in performance of the symptomatic HD group reflect a deficit in judgment and/ or inhibition of response deficits. Importantly there are actual deficits on the tasks examined which are consistent with the reports in a clinical setting of impaired judgment and changes in social behaviour in HD populations.

CONCLUSION

People with HD do appear to display quantifiable deficits in decision-making and judgement as measured using a gambling task and a ToM task requiring the detection of faux pas. The performance of the HD group was consistent with the findings of previous research (Stout et al, 2001). The faux pas task had not been used with a HD population prior to this study but the performance of the symptomatic HD group certainly would warrant further investigation as would the performance of the presymptomatic HD gene carriers on the faux pas task. There was a greater variability in the performance of the individuals in the presymptomatic group than the control group. Performance of individuals on these tasks does however appear to be consistent with their current level of function.

Previous research has suggested that deficits on gambling-task may result from underlying memory impairments (Stout et al., 2001) though this study did not entirely support this. Therefore it might be that the main explanation for the apparent deficits of the symptomatic HD participants on the gambling task is impaired judgement.

The performance of the HD participants on the faux pas task was associated with memory. However this task did not have a memory loading and therefore further research is required to investigate this apparent association. Noticeably the performance of the control group was also associated with memory suggesting there is an involvement of this function.

The final hypothesis investigated if there was any relationship between the two main measures investigated. There was found to be a trend in association between the number of advantageous decks selected and performance on the faux pas task, which perhaps reflects the involvement of the same frontal sub-cortical circuitry (Cummings, 1993).

CHAPTER FIVE

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APPENDICES

APPENDIX ONE

Patient Information Sheet
&
Consent Form

17/10/00 (Nr 1)

PATIENT INFORMATION SHEET

Social Judgment and Risk Taking Behaviour in People with Huntington's Disease

You are being invited to participate in a research study. Before you make a decision it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and you G.P if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

1. What is the purpose of the study?

The present study is part of a Clinical Psychology thesis, which aims to investigate different aspects of behaviour. The aspects to be investigated include social judgment and risk taking behaviour, together with an investigation of the level of stress experienced by individuals involved in your care (if appropriate). Also included in the study are cognitive assessments, which examine individuals' cognitive strengths and weaknesses. The study hopes to provide additional information about the nature of Huntington's Disease, however it does not aim to be diagnostic in any sense. If you decide to participate, you will be required to attend one appointment, which will last approximately 1 hour.

2. Why have I been chosen?

In order to find out more about Huntington's Disease, we are interested in studying changes in the nature of the disease. Thus these assessments will be carried out with approximately 14 individuals who have recently been identified through genetic testing as having the Huntington's disease mutated gene, and 14 individuals who have actually been diagnosed with Huntington's disease. The assessment will also be given to 14 individuals who do not have the Huntington's Disease gene.

3. Do I have to take part?

It is up to you if you decide whether or not to take part. If you decide not to take part this will not in anyway affect the care you receive. If however you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Any decisions you make either prior to, or during the study, regarding your participation, will not affect the care you receive.

4. What will happen to me if I take part?

If you decide to participate in the study you will be required to complete two psychological tests. One test will require you to listen to short stories and you will be asked questions about the person in the story as I read it to you. The other test will involve a computer-generated task, when you will be required to select a card from a set of four on a screen. Throughout the session it is important that you concentrate on the task.

You will also be asked to complete a number of short cognitive assessments. These assessments will require you to respond to a number of questions, to reconstruct certain patterns, identify different patterns, to remember a short story together with naming tasks.

There are also three short questionnaires, which you will be asked to complete, that ask you to rate your mood and behaviour. These questionnaires will be returned to the researcher following your appointment.

With your permission an individual involved in your care or someone close to you will be asked to complete three similar short questionnaires. Please specify the name and address of the individual you would like us to contact:

Name:.....
Address: .....
.....
.....
Tel No.: .....

5. Feedback on your performance

Once you have completed the assessments time will be allowed for you to ask questions about your performance. The researcher will give you feedback about your performance in general. However specific feedback about your performance on a particular tests, will not be available until the researcher has taken the assessments away and scored them. If you have particular concerns about your performance, a follow-up appointment will be offered by the researcher to discuss these concerns.

6. What are the possible disadvantages and risks of taking part?

There are no risks associated with participating in this study.

7. What are the possible benefits of taking part?

There is no clinical benefit to be gained from you taking part in this study. However as mentioned it will hopefully give us a greater understanding of the course and nature of Huntington's Disease and perhaps help others to understand the nature of your difficulties.

8. What if something goes wrong?

If you feel the person responsible for this study has treated you inappropriately, or the experiment caused you distress then please make this known to the researcher themselves or perhaps to the Scottish Huntington's disease Advisory Service, (SHDAS) advisor ie Marie McGill or Roger Irwin.

9. Will my taking part be confidential?

If you consent to take part in the research, the researcher may inspect your medical records for the purposes of analyzing the results. All information, which is collected, about you during the course of research will be kept strictly confidential. However your G.P, will be contacted and informed of your participation in the study. Any information about you, which does leave the clinic, you attend, will have your name and address removed so that you cannot be recognised from it.

10. What will happen to the results of the research study?

The information collected will be used for writing an academic piece of work and perhaps for publication in a scientific journal. In these instances, no information about the identity of the participants will be included in any subsequent reports.

11. Who is organising and funding the research?

The present study is part of a D.Clin.Psych thesis, of a doctorate of Clinical Psychology. The research is carried out as part of her employment requirements. The principal researcher is a Clinical Psychologist in Training, Fife Primary Care NHS Trust and University of Edinburgh.

12. Who has reviewed the study?

The study has been reviewed by the Fife Health Board Local Research Ethics Committee together with Professor M Power, Department of Clinical Psychology, University of Edinburgh and Lothian Research and Ethics Committee.

13. Contact for Further Information

If you would like any further information then please contact:

Mhorag Paul
Clinical Psychologist in Training
Dept of Clinical Psychology
Stratheden Hospital
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Fife
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Local Advisors:

Marie McGill/ Roger Irwin
Huntington's Advisors
Scottish Huntington's Disease Advisory Service
South East of Scotland Clinical Genetic Service
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0131 536 9050

Professor Ronan O'Carrol
Psychology Department
University of St Andrews
St Andrews

Please keep this information sheet and the signed consent form

Study Number:
Patient Identification Number for this trial:

CONSENT FORM

Title of Project:

The Relationship between Social Cognition, Risk-taking Behaviour, and Carer Stress in Patients with Huntington's Disease.

Name of Researcher: Mhorag Paul

Please initial box

1. I confirm that I have read and understand the information sheet dated 17/10/00 Version Nr1 for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that sections of any of my medical notes may be looked at by responsible individuals from the health service or university staff, where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐
4. I understand that my G.P, will be informed of my participation in this study. ☐
5. I agree to take part in the above study ☐

Name of patient	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

1 for patient; 1 for researcher; 1 to be kept with hospital notes

Appendix Two

Faux Pas Task

(Stories 1-20)

V. Stone FP test
S.Baron-Cohen

1. Vicky was at a party at her friend Oliver's house. She was talking to Oliver when another woman came up to them. She was one of Oliver's neighbors. The woman said, "Hello," then turned to Vicky and said, " I don't think we've met. I'm Maria, what's your name?" "I'm Vicky." "Would anyone like something to drink?" Oliver asked.

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Vicky felt?

Control questions: In the story, where was Vicky?

Did Vicky and Maria know each other?

2. Helen's husband was throwing a surprise party for her birthday. He invited Sarah, a friend of Helen's, and said, "Don't tell anyone, especially Helen." The day before the party, Helen was over at Sarah's and Sarah spilled some coffee on a new dress that was hanging over her chair. "Oh!" said Sarah, "I was going to wear this to your party!" "What party?" said Helen. "Come on," said Sarah, "Let's go see if we can get the stain out."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Helen felt?

Control question: In the story, who was the surprise party for?

3. Jim was shopping for a shirt to match his suit. The salesman showed him several shirts. Jim looked at them and finally found one that was the right color. But when he went to the dressing room and tried it on, it didn't fit. "I'm afraid it's too small," he said to the salesman. "Not to worry," the salesman said. "We'll get some in next week in a larger size." "Great. I'll just come back then," Jim said.

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Jim felt?

Control question: In the story, what was Jim shopping for?

Why was he going to come back next week?

4. Jill had just moved into a new apartment. Jill went shopping and bought some new curtains for her bedroom. When she had just finished decorating the apartment, her best friend, Lisa, came over. Jill gave her a tour of the apartment and asked, "How do you like my bedroom?" "Those curtains are horrible," Lisa said. "I hope you're going to get some new ones!"

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Jill felt?

Control question: In the story, what had Jill just bought?

V. Stone FP test
S.Baron-Cohen

5. Bob went to the barber for a haircut. "How would you like it cut?" the barber asked. "I'd like the same style as I have now, only take about an inch off," Bob replied. The barber cut it a little uneven in the front, so he had to cut it shorter to even it out. "I'm afraid it's a bit shorter than you asked for," said the barber. "Oh well," Bob said, "it'll grow out."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Bob felt?

Control question: In the story, how did Bob want his hair cut?

How did the barber cut his hair?

6. John stopped off at the gas station on the way home to fill up his car. He gave the cashier his credit card. The cashier ran it through the machine at the counter. "I'm sorry," she said, "the machine won't accept your card." "Hmmm, that's funny," John said. "Well, I'll just pay in cash." He gave her twenty dollars and said, "I filled up the tank with unleaded."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think John felt?

Control question: In the story, what did John stop off to buy?

Why did he pay in cash?

7. Sally is a three-year-old girl with a round face and short blonde hair. She was at her Aunt Carol's house. The doorbell rang and her Aunt Carol answered it. It was Mary, a neighbor. "Hi," Aunt Carol said, "Nice of you to stop by." Mary said, "Hello," then looked at Sally and said, "Oh, I don't think I've met this little boy. What's your name?"

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Sally felt?

Control question: In the story, where was Sally?

8. Joan took her dog, Zack, out to the park. She threw a stick for him to chase. When they had been there a while, Pam, a neighbor of hers, passed by. They chatted for a few minutes. Then Pam asked, "Are you heading home? Would you like to walk together?" "Sure," Joan said. She called Zack, but he was busy chasing pigeons and didn't come. "It looks like he's not ready to go," she said. "I think we'll stay." "OK," Pam said. "I'll see you later."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Pam felt?

Control question: In the story, where had Joan taken Zack?

Why didn't she walk with her friend Pam?

9. Joanne had had a major role in last year's school play and she really wanted the lead role this year. She took acting classes, and in the spring, she auditioned for the play. The day the decisions were posted, she went before class to check the list of who had made the play. She hadn't made the lead and had instead been cast in a minor role. She ran into her boyfriend in the hall and told him what had happened. "I'm sorry," he said. "You must be disappointed." "Yes," Joanne answered, "I have to decide whether to take this role."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Joanne felt?

Control question: In the story, what role did Joanne get?

What kind of role had she had the previous year?

What did her boyfriend say?

10. Joe was at the library. He found the book he wanted about hiking in the Grand Canyon and went up to the front counter to check it out. When he looked in his wallet, he discovered he had left his library card at home. "I'm sorry," he said to the woman behind the counter. "I seem to have left my library card at home." "That's OK," she answered. "Tell me your name, and if we have you in the computer, you can check out the book just by showing me your driver's license."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Joe felt?

Control question: In the story, what book did Joe get at the library?

Was he going to be able to check it out?

11. Jean West, the president of Abco Corporation, called a meeting for all of the senior executives. "I have something to tell you," she said. "John Morehouse, one of our vice-presidents, is very sick with cancer and he's in the hospital." Everyone was quiet, absorbing the news, when Robert, one of the management team arrived late. "Hey, I heard this great joke last night! What did the terminally ill patient say to his doctor?" Jean West said, "Okay, let's get down to business in the meeting."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Jean West felt?

Control question: In the story, what did Jean West tell the people in the meeting?

12. Mike, a nine-year-old boy, just started at a new school. He was in one of the stalls in the restroom at school. Joe and Peter, two other boys, came in and were standing at the sinks talking. Joe said, "You know that new guy in the class? His name's Mike. Doesn't he look weird? And he's so short!" Mike came out of the stall and Joe and Peter saw him. Peter said, "Oh hi, Mike! Are you going out to play football now?"

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Mike felt?

Control question: In the story, where was Mike while Joe and Peter were talking?

13. Kim's cousin, Joe, was coming to visit and Kim made an apple pie especially for him. After dinner, she said, "I made a pie just for you. It's in the kitchen." "Mmmm," replied Joe, "It smells great! I love pies, except for apple, of course."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Kim felt?

Control question: In the story, what kind of pie did Kim make?

V. Stone FP test
S.Baron-Cohen

14. Jeanette bought her friend, Anne, a crystal bowl for a wedding gift. Anne had a big wedding and there were a lot of presents to keep track of. About a year later, Jeanette was over one night at Anne's for dinner. Jeanette dropped a wine bottle by accident on the crystal bowl and the bowl shattered. "I'm really sorry. I've broken the bowl," said Jeanette. "Don't worry," said Anne. "I never liked it anyway. Someone gave it to me for my wedding."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Jeanette felt?

Control question: In the story, what did Jeanette give Anne for her wedding?

15. At Fernhaven Elementary School, there was a story competition. Everyone was invited to enter. Several of the fifth graders did so. Christine, a fifth grader, loved the story she had entered in the competition. A few days later, the results of the competition were announced: Christine's story had not won anything and a classmate, Jake, had won first prize. The following day, Christine was sitting on a bench with Jake. They were looking at his first prize trophy. Jake said, "It was so easy to win that contest. All of the other stories in the competition were terrible." "Where are you going to put your trophy?" asked Christine.

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Christine felt?

Control question: In the story, did Christine enter the contest?

Who won the contest?

16. Tim was in a restaurant. He spilled some coffee on the floor by accident. "I'll get you another cup of coffee," said the waiter. The waiter was gone for a while. Jack was another customer in the restaurant, standing by the cashier waiting to pay. Tim went up to Jack and said, "I spilled coffee over by my table. Can you mop it up?"

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Jack felt?

Control question: In the story, why was Jack standing by the cashier?

17. Eleanor was waiting at the bus stop. The bus was late and she had been standing there a long time. She was 65 and it made her tired to stand for so long. When the bus finally came, it was crowded and there were no seats left. She saw a neighbor, Peter, standing in the aisle of the bus. "Hello, Eleanor," he said. "Were you waiting there long?" "About 20 minutes," she replied. A young man who was sitting down got up. "Ma'am, would you like my seat?"

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Eleanor felt?

Control question: In the story, why was Eleanor waiting at the bus stop for 20 minutes?

Were there any seats available on the bus when she got on?

V. Stone FP test
S.Baron-Cohen

18. Robert had just started work at a new office. One day, in the coffee room, he was talking to a new friend, Andrew. "What does your wife do?" Andrew asked. "She's a lawyer," answered Robert. A few minutes later, Claire came into the coffee room looking irritated. "I just had the worst phone call," she told them. "Lawyers are all so arrogant and greedy. I can't stand them." "Do you want to come look over these reports?" Andrew asked Claire. "Not now," she replied, "I need my coffee."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Robert felt?

Control question: In the story, what does Robert's wife do for a living?

19. Richard bought a new car, a red Peugeot. A few weeks after he bought it, he backed it into his neighbor's car, an old beat-up Volvo. His new car wasn't damaged at all and he didn't do much damage to his neighbor's car either -- just a scratch in the paint above the wheel. Still, he went up and knocked on the door. When his neighbor answered, Richard said, "I'm really sorry. I've just put a small scratch on your car." The neighbor looked at it and said, "Don't worry. It was only an accident."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think the neighbor felt?

Control question: In the story, what did Richard do to his neighbor's car?

How did his neighbor react?

V. Stone FP test
S.Baron-Cohen

20. Louise went to the butcher to buy some meat. It was crowded and noisy in the shop. She asked the butcher, "Do you have any range-fed chickens?" He nodded and started to wrap up a roasted chicken for her. "Excuse me," she said, "I must not have spoken clearly. I asked if you had any range-fed chickens." "Oh, sorry," the butcher said, "we're all out of them."

Did anyone say something they shouldn't have said or something awkward?

If yes, ask:
Who said something they shouldn't have said or something awkward?

Why shouldn't he/she have said it or why was it awkward?

Why do you think he/she said it?

How do you think Louise felt?

Control question: In the story, where did Louise go?

Why did the butcher start to wrap up a roasted chicken for her?

APPENDIX THREE

Additional Results

Results of Analysis Using Non Parametric and Parametric Statistics
&
Post-Hoc Comparison Tables

Results of Analysis Using Non Parametric Statistics

The following tables contain the results of analysis using nonparametric statistics. As revealed if a statistically significant result was achieved using parametric methods it was also achieved using non-parametric methods. There is therefore a statistically significant difference on measure of IQ $p < 0.05$. The groups also differ significantly differ on performance on the faux pas task (FP) $p < 0.01$, but not on the empathy question $p > 0.1$. To the researcher knowledge there is no way to control for IQ when using non-parametric statistics on SPSS.

The faux pas task was also broken down to examine the performance on each question, which gave the overall FP score. As multiple comparisons were being carried out the Bonferroni correction was used and therefore the p value must be less than $p < 0.0125$ to achieve significance. Therefore the difference in performance of the symptomatic, presymptomatic and control groups on question 3 was statistically significant.

With regard to the analysis of the data on the gambling task, there is not a equivalent test to examine a deck by group interaction. However there was an effect of deck using Friedman's analysis $p < 0.01$.

Table 12 (a & b) Results of the Krucal-Wallis Test Examining the Different IQ scores on the WASI-2 for the symptomatic and presymptomatic HD groups and controls

(a)

Ranks

	Group	N	Mean Rank
IQII	1.00 symptomatic	14	12.46
	2.00 presymptomatic	10	21.05
	3.00 control	13	24.46
	Total	37	

(b)

Test Statistics[a,b]

	IQII
Chi-Square	8.782
df	2
Asymp. Sig.	.012

a. Kruskal Wallis Test

b. Grouping Variable: Group

Table 13. (a & b) Results of the Kruscal-Wallis Examining the Between Group Differences on the Theory of Mind Faux Pas Task and Empathy Question.

(a)

Ranks

	Group	N	Mean Rank
TOMFP	1.00 symptomatic	10	10.70
	2.00 presymptomatic	10	14.65
	3.00 control	13	23.65
	Total	33	
TOMEMP	1.00 symptomatic	10	13.00
	2.00 presymptomatic	10	18.40
	3.00 control	13	19.00
	Total	33	

(b)

Test Statistics[a,b]

	TOMFP	TOMEMP
Chi-Square	11.078	2.849
df	2	2
Asymp. Sig.	.004	.241

a. Kruskal Wallis Test

b. Grouping Variable: Group

Table 14. (a & b). Results of the Kruscal-Wallis, examining between group differences on each question of the Faux Pas Task.

(a)

Ranks

	Group	N	Mean Rank
QUES1FP	1.00 symptomatic	10	21.95
	2.00 presymptomatic	10	17.90
	3.00 control	13	12.50
	Total	33	
QUES2FP	1.00 symptomatic	10	18.20
	2.00 presymptomatic	10	18.40
	3.00 control	13	15.00
	Total	33	
QUES3FP	1.00 symptomatic	10	22.80
	2.00 presymptomatic	10	16.40
	3.00 control	13	13.00
	Total	33	
QUES4FP	1.00 symptomatic	10	18.90
	2.00 presymptomatic	10	20.25
	3.00 control	13	13.04
	Total	33	

(b)

Test Statistics[a,b]

	QUES1FP	QUES2FP	QUES3FP	QUES4FP
Chi-Square	6.705	2.867	10.382	3.813
df	2	2	2	2
Asymp. Sig.	.035	.239	.006	.149

a. Kruskal Wallis Test

b. Grouping Variable: Group

Table 15. (a & b) Friedman Test Examining Effect of Deck

(a)

Ranks

	Mean Rank
A	1.93
B	3.23
C	2.14
D	2.70

(b)

Test Statistics[a]

N	37
Chi-Square	23.606
df	3
Asymp. Sig.	.000

a. Friedman Test

Parametric Correlations

With regard to the analysis relating to hypotheses 3 and 4, which examined the associations between different measures, the results of the non-parametric statistics were given in the results. The results using Pearson's Correlation are displayed in Table. 16. There is a significant contrast between the associations using nonparametric and parametric analysis.

Table 16. Correlations of the sum of advantageous selections over decks 61-100 with general level of function, verbal memory and executive functioning using Pearson's Correlation (*r*).

	Symptomatic HD	Presymptomatic HD	Controls
WASI-IQ 2	0.152 p = 0.604	0.354 p = 0.315	0.031 p = 0.920
Stroop	0.588 p = 0.044	0.033 p = -1.109	-0.101 p = 0.742
Story Recall Immediate (AMIPB)	0.577 p = 0.031	0.061 p = 0.867	-0.205 p = 0.502
Story Recall Delayed (AMIPB)	0.563 p = 0.036	0.326 p = 0.358	-0.224 p = 0.461
Letter Fluency	0.160 p = 584	0.638 p = 0.047	-0.052 p = 0.866
Semantic Fluency	-0.341 p = 0.233	-0.021 p = 0.954	-0.08 p = 0.796
Theory of Mind Faux Pas	0.624 p = 0.053	0.928 p = 0.765	-0.025 p = 0.936

The results of the parametric analysis are similar to comparisons carried out by Stout et al. 2001. In the symptomatic HD the number of advantageous selections (from decks C & D) summed across selections 61-100 were not significantly correlated with general intellectual functioning as measured by the IQ-2 from the WASI, $r = 0.152$, p 0.604. Performance in selections 61-100, was however significantly correlated with measures of executive function and memory. The number of advantageous selections correlated significantly with verbal memory immediate $r = 0.577$, $p < 0.05$, delayed $r = 0.563$, $p < 0.05$, and the Stroop $r = 0.588$, $p < 0.05$ in the symptomatic HD group. There were no significant associations with letter or semantic fluency $p > 0.1$. There were no associations between these factors when the scores were ranked and analysed using Spearman's rank order correlation.

In the presymptomatic HD there was interestingly a correlation between advantageous choices and letter fluency $r = 0.638$, $p < 0.05$. This correlation was not found using Spearman's Rank Correlation.

With regard to hypothesis 4 there was no association found between the number of advantageous selections and performance on the faux pas task in any of the groups, ($p > 0.05$).

Post Hoc Comparisons

The post hoc comparisons look at where the significant differences lay between the groups on the faux pas task, the tests of executive function, IQ and memory. The post hoc comparisons were carried out on the parametric ANOVA analysis.

Table 17. Post Hoc Comparisons of WASI-2, IQ Score.

Multiple Comparisons

Dependent Variable: IQII

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	1.00 symptomatic	2.00 presymptomatic	-15.06	7.02	.096	-32.26	2.15
		3.00 control	-21.28*	6.53	.007	-37.29	-5.27
	2.00 presymptomatic	1.00 symptomatic	15.06	7.02	.096	-2.15	32.26
		3.00 control	-6.22	7.13	.661	-23.70	11.26
	3.00 control	1.00 symptomatic	21.28*	6.53	.007	5.27	37.29
		2.00 presymptomatic	6.22	7.13	.661	-11.26	23.70
Scheffe	1.00 symptomatic	2.00 presymptomatic	-15.06	7.02	.116	-33.03	2.92
		3.00 control	-21.28*	6.53	.010	-38.00	-4.56
	2.00 presymptomatic	1.00 symptomatic	15.06	7.02	.116	-2.92	33.03
		3.00 control	-6.22	7.13	.686	-24.48	12.04
	3.00 control	1.00 symptomatic	21.28*	6.53	.010	4.56	38.00
		2.00 presymptomatic	6.22	7.13	.686	-12.04	24.48

*. The mean difference is significant at the .05 level.

Table 18. Post Hoc Comparisons of the Faux Pas Task

Multiple Comparisons

Dependent Variable: TOMFP

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	1.00 symptomatic	2.00 presymptomatic	-5.20	3.06	.221	-12.74	2.34
		3.00 control	-10.35*	2.87	.003	-17.44	-3.27
	2.00 presymptomatic	1.00 symptomatic	5.20	3.06	.221	-2.34	12.74
		3.00 control	-5.15	2.87	.189	-12.24	1.93
	3.00 control	1.00 symptomatic	10.35*	2.87	.003	3.27	17.44
		2.00 presymptomatic	5.15	2.87	.189	-1.93	12.24
Scheffe	1.00 symptomatic	2.00 presymptomatic	-5.20	3.06	.251	-13.07	2.67
		3.00 control	-10.35*	2.87	.005	-17.76	-2.95
	2.00 presymptomatic	1.00 symptomatic	5.20	3.06	.251	-2.67	13.07
		3.00 control	-5.15	2.87	.217	-12.56	2.25
	3.00 control	1.00 symptomatic	10.35*	2.87	.005	2.95	17.76
		2.00 presymptomatic	5.15	2.87	.217	-2.25	12.56

Based on observed means.

*. The mean difference is significant at the .05 level.

Table 19. Post Hoc Comparisons of the Stroop

Multiple Comparisons

Dependent Variable: STROOP

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	1.00 symptomatic	2.00 presymptomatic	-39.93*	9.30	.000	-62.78	-17.09
		3.00 control	-39.49*	8.69	.000	-60.84	-18.13
	2.00 presymptomatic	1.00 symptomatic	39.93*	9.30	.000	17.09	62.78
		3.00 control	.45	9.13	.999	-21.99	22.89
	3.00 control	1.00 symptomatic	39.49*	8.69	.000	18.13	60.84
		2.00 presymptomatic	-.45	9.13	.999	-22.89	21.99
Scheffe	1.00 symptomatic	2.00 presymptomatic	-39.93*	9.30	.001	-63.79	-16.07
		3.00 control	-39.49*	8.69	.000	-61.79	-17.18
	2.00 presymptomatic	1.00 symptomatic	39.93*	9.30	.001	16.07	63.79
		3.00 control	.45	9.13	.999	-22.99	23.89
	3.00 control	1.00 symptomatic	39.49*	8.69	.000	17.18	61.79
		2.00 presymptomatic	-.45	9.13	.999	-23.89	22.99

Based on observed means.

*. The mean difference is significant at the .05 level.

Table20. Post Hoc Comparisons of Letter Fluency (Corrected)

Multiple Comparisons

Dependent Variable: VFCORR

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	1.00 symptomatic	2.00 presymptomatic	-14.93*	4.93	.013	-27.01	-2.85
		3.00 control	-20.43*	4.59	.000	-31.67	-9.19
	2.00 presymptomatic	1.00 symptomatic	14.93*	4.93	.013	2.85	27.01
		3.00 control	-5.50	5.01	.522	-17.77	6.77
	3.00 control	1.00 symptomatic	20.43*	4.59	.000	9.19	31.67
		2.00 presymptomatic	5.50	5.01	.522	-6.77	17.77
Scheffe	1.00 symptomatic	2.00 presymptomatic	-14.93*	4.93	.017	-27.55	-2.31
		3.00 control	-20.43*	4.59	.000	-32.17	-8.69
	2.00 presymptomatic	1.00 symptomatic	14.93*	4.93	.017	2.31	27.55
		3.00 control	-5.50	5.01	.553	-18.32	7.32
	3.00 control	1.00 symptomatic	20.43*	4.59	.000	8.69	32.17
		2.00 presymptomatic	5.50	5.01	.553	-7.32	18.32

Based on observed means.

*. The mean difference is significant at the .05 level.

Table 21. Post Hoc Comparisons of Semantic/Category Fluency.

Multiple Comparisons

Dependent Variable: SVFI

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	1.00 symptomatic	2.00 presymptomatic	-3.83	2.47	.282	-9.89	2.24
		3.00 control	-10.35*	2.30	.000	-15.99	-4.71
	2.00 presymptomatic	1.00 symptomatic	3.83	2.47	.282	-2.24	9.89
		3.00 control	-6.52*	2.51	.036	-12.68	-.36
	3.00 control	1.00 symptomatic	10.35*	2.30	.000	4.71	15.99
		2.00 presymptomatic	6.52*	2.51	.036	.36	12.68
Scheffe	1.00 symptomatic	2.00 presymptomatic	-3.83	2.47	.315	-10.16	2.51
		3.00 control	-10.35*	2.30	.000	-16.24	-4.46
	2.00 presymptomatic	1.00 symptomatic	3.83	2.47	.315	-2.51	10.16
		3.00 control	-6.52*	2.51	.046	-12.96	-8.77E-02
	3.00 control	1.00 symptomatic	10.35*	2.30	.000	4.46	16.24
		2.00 presymptomatic	6.52*	2.51	.046	8.77E-02	12.96

Based on observed means.

*. The mean difference is significant at the .05 level.

Table 22. Post Hoc Comparisons of Story Recall (Immediate)

Multiple Comparisons

Dependent Variable: SRIMM

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	1.00 symptomatic	2.00 presymptomatic	-17.11*	4.77	.003	-28.80	-5.43
		3.00 control	-17.48*	4.44	.001	-28.36	-6.61
	2.00 presymptomatic	1.00 symptomatic	17.11*	4.77	.003	5.43	28.80
		3.00 control	-.37	4.85	.997	-12.24	11.50
	3.00 control	1.00 symptomatic	17.48*	4.44	.001	6.61	28.36
		2.00 presymptomatic	.37	4.85	.997	-11.50	12.24
Scheffe	1.00 symptomatic	2.00 presymptomatic	-17.11*	4.77	.004	-29.32	-4.91
		3.00 control	-17.48*	4.44	.002	-28.84	-6.13
	2.00 presymptomatic	1.00 symptomatic	17.11*	4.77	.004	4.91	29.32
		3.00 control	-.37	4.85	.997	-12.77	12.03
	3.00 control	1.00 symptomatic	17.48*	4.44	.002	6.13	28.84
		2.00 presymptomatic	.37	4.85	.997	-12.03	12.77

*. The mean difference is significant at the .05 level.

Table 23. Post Hoc Comparisons of Story Recall (Delayed).

Multiple Comparisons

Dependent Variable: SRDEL

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	1.00 symptomatic	2.00 presymptomatic	-15.11*	4.97	.012	-27.29	-2.94
		3.00 control	-17.87*	4.62	.001	-29.20	-6.54
	2.00 presymptomatic	1.00 symptomatic	15.11*	4.97	.012	2.94	27.29
		3.00 control	-2.75	5.05	.849	-15.13	9.62
	3.00 control	1.00 symptomatic	17.87*	4.62	.001	6.54	29.20
		2.00 presymptomatic	2.75	5.05	.849	-9.62	15.13
Scheffe	1.00 symptomatic	2.00 presymptomatic	-15.11*	4.97	.017	-27.84	-2.39
		3.00 control	-17.87*	4.62	.002	-29.70	-6.03
	2.00 presymptomatic	1.00 symptomatic	15.11*	4.97	.017	2.39	27.84
		3.00 control	-2.75	5.05	.862	-15.68	10.17
	3.00 control	1.00 symptomatic	17.87*	4.62	.002	6.03	29.70
		2.00 presymptomatic	2.75	5.05	.862	-10.17	15.68

*. The mean difference is significant at the .05 level.

Variance Tables

The tables below give the explained variance between the different measures used in the study.

Table 24. Measure of Predictable Variability of Number of Advantageous Deck Selections with Tests of Executive Function and Memory (r^2)

	Symptomatic HD	Presymptomatic HD	Controls
WASI-IQ 2	0.0225	9	0.90
Stroop	24.6	0.04	0.18
Story Recall Immediate (AMIPB)	20.88	0.036	2.46
Story Recall Delayed (AMIPB)	19.01	13.62	3.53
Letter Fluency	0.01	32.26	0.42
Semantic Fluency	11.97	0.10	1.69
Theory of Mind Faux Pas	52.12	1.32	0.014

Table 25. Predictable Variation in Performance on Tests of Executive Function and Memory from Performance in the Faux Pas task (r^2)

	Symptomatic	Presymptomatic	Control
WASI-2 (I.Q)	26.21	5.15	70.9
Stroop	58.06	26.73	24.4
Story Recall (Immediate)	56.25	1.72	42.51
Story Recall (Delayed)	53.44	1.82	56.10
Letter Fluency	2.5	0.96	28.62
Semantic Fluency	0.35	17.14	29.7